INTRAVASCULAR ULTRASOUND AND PERIPHERAL ENDOVASCULAR INTERVENTIONS

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INTRAVASCULAIRE ECHOGRAFIE EN PERIFERE

ENDOVASCULAIRE INTERVENTIES

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CHAPTER 1

INTRODUCTION

Endovascular interventions and vascular imaging.

In recent years the interest in minimal invasive surgery has been growing and the same trend can be observed in vascular surgery, leading to what is commonly referred to as "endovascular surgery". Although the 1990s represent an era of technical revolution in vascular surgery, it is a misunderstanding to consider endovascular treatment a recent development. In 1947 João Cid dos Santos described the thrombo-endarterectomy[1]; this technique was modified by Vollmar in 1964, to a semi-closed endarterectomy using ring-strippers.[2] In the same year other pioneers, including Dotter and Judkins, published preliminary results on what they called "angioplasty" of the femoropopliteal artery using co-axial catheters.[3] This technique was later modified by Grüntzig in 1974, who replaced the co-axial catheters with dilatation balloons.[4] In the early 1990s, Volodos and Parodi introduced the endovascular treatment of the abdominal aortic aneurysm with a device composed of a Dacron graft and Palmaz stents.[5,6]

The collaboration between interventional radiologists and vascular surgeons has been of eminent importance for further evolution of endovascular techniques. Nowadays a great variety of obstructive and aneurysmal peripheral vascular diseases can be treated with catheter-guided, endovascular and, therefore, less invasive techniques.

The development of these endovascular techniques prompted the need for improved vascular imaging and better diagnostics. Since angiography displays only a "lumenogram" of the vessel, this precludes qualitative evaluation of atherosclerotic plaque and quantitative assessment of plaque and vessel. Sophisticated modalities such as colour duplex, computed tomographic angiography and magnetic resonance imaging can be important in the pre- and postintervention assessment of vascular disease. These techniques, however, do not always give accurate information on the dimensions of the vessel or the extent of the disease and at the present time cannot be used during intervention.[7] Intravascular ultrasound depicts both the vascular lumen and vascular wall: thus, information can be obtained on the atheromatous plaque constituents and the size of the lumen, vessel wall and arterial disease.

History of intravascular ultrasound

Reports on intraluminal ultrasound date back to the 1950s. Acoustic elements were mounted on either a catheter tip or a gastroscopic pipe. The low sensitivity of the early external ultrasound transducers, and the associated need for close proximity to the organs to be studied, were the main reasons for the development of this endoluminal technique. In 1956 Cieszynski et al.[8] developed an ultrasonic catheter for intra-cardiac use. This enabled to obtain ultrasonic reflections of the heart during pig-model experiments. In 1966 Kossoff and co-workers described an ultrasonic catheter of 2 mm in diameter with an operating frequency of 8 MHz: this device allowed measurement of the septal and ventricular wall thickness of the heart with an accuracy of 0.1 mm.[9] In the same year Wells et al.[10] reported on the use of a 3-mm diameter, 1.5 MHz ultrasound catheter which he used in human veins.

In 1972 Bom et al.[11] described an electronically switched phased array system that contains 32 small acoustic, 5.5 MHz elements that are positioned cylindrically around the catheter tip: each transducer element transmits and receives ultrasound waves independently (Fig. 1). This device was used in a pig model for cardiac application. It took another 15 years before higher frequency ultrasound transducers (30 MHz) became available, providing more detailed images. Because these transducers were small, they could be mounted into a smaller diameter catheter for intravascular application.

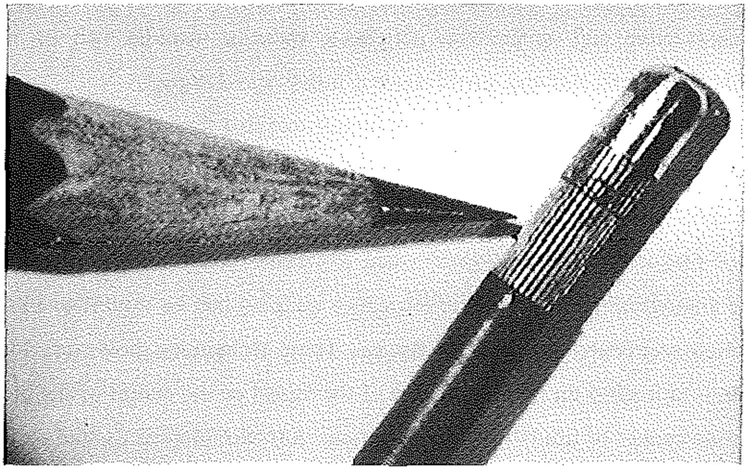

Figure 1. The phased array 32-element catheter tip as described by Bom in the early seventies. (Adapted from: Intravascular Ultrasound: techniques, developments, clinical perspectives. Bom N, Roelandt J (Eds). Kluwer Academic Publishers, Dordrecht 1989. With permission from the author).

Besides the electronically switched phase array system, 2 other intravascular ultrasound systems were developed at that time: 1) the mechanical rotating mirror system, consisting of a non-moving ultrasound transducer in combination with a rotating mirror, which deflects the ultrasound waves emitted by the single element (Fig. 2) and; 2) a mechanical system, similar to the latter one, but instead of a mirror a single element is rotating (Fig. 3).[12] Interference of the transducer holder and the ultrasound beam creates a dropout in the ultrasound image in the rotating mirror system, a problem that is not encountered in the rotating element system.

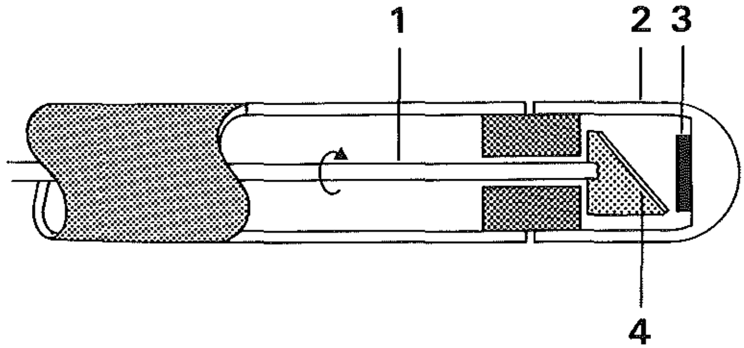

Figure 2. Mechanically driven echo catheter tip with mirror. Rotating shaft (1), transparent dome (2), echo element (3) and rotating mirror (4). (Adapted from: Intravascular Ultrasound: techniques, developments, clinical perspectives. Bom N, Roelandt J (Eds). Kluwer Academic Publishers, Dordrecht 1989. With permission from the author).

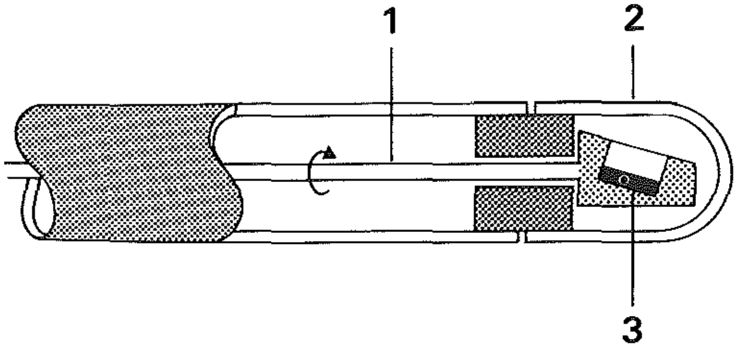

Figure 3. Echo catheter with rotating element. Rotating shaft (1), transparent dome (2) and rotating echo element (3). (Adapted from: Intravascular Ultrasound: techniques, developments, clinical perspectives. Bom N, Roelandt J (Eds). Kluwer Academic Publishers, Dordrecht 1989. With permission from the author).

Scope of this thesis

The intravascular ultrasound studies described in this dissertation were performed with a mechanical system (Endosonics, Rijswijk, the Netherlands). The 4.3 French catheter used contains a 1-mm diameter, 30 MHz transducer that is rotated externally using a motor. In this thesis the contribution of intravascular ultrasound to improve immediate results, reduce complications, prevent restenosis and increase long-term patency in peripheral endovascular interventions is discussed and evaluated in 2 categories of patients.

Section 1 addresses patients with documented obstructive vascular disease treated with percutaneous transluminal angioplasty, stent placement or an endograft.

Section 2 deals with patients with a peripheral aneurysm treated with a stent-graft combination.

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CHAPTER 2

IS THE USE OF INTRAVASCULAR ULTRASOUND ESSENTIAL FOR FEMOROPOPLITEAL BALLOON ANGIOPLASTY AND STENTING?

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Introduction

Balloon angioplasty is a widely used technique for obstructive disease in the femoropopliteal artery. However, there seems to be a discrepancy between the initial angiographic success and the disappointingly high incidence of restenosis (1 year patency rates: 47-73%).[1,2] This promoted the development of alternative endovascular interventions. Parallel with this development there is a need for improved vascular imaging and better diagnostics. Whereas angiography displays a longitudinal silhouette of the vessel lumen, intravascular ultrasound (IVUS) provides histology- like cross-sectional images of the blood vessel, allowing qualitative evaluation of plaque morphology and quantitative measurement of lumen and plaque area by topographic imaging[3-5] (Fig. 1).

Our institution has experience with over 400 endovascular cases in which IVUS was used to guide a variety of vascular interventions.

In this chapter the advantages of IVUS over angiography, the mechanism of balloon angioplasty and stent placement, some aspects of the mechanism of restenosis and the IVUS predictors of restenosis will be addressed.

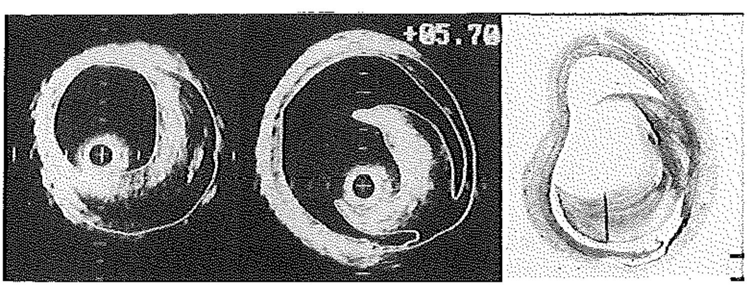

Figure 1. Intravascular ultrasound (IVUS) images of the femoropopliteal artery obtained *in vitro* before and after balloon angioplasty and corresponding histologic section. As a result of the intervention lumen area increase was associated with a dissection. The IVUS cross-sections are contour traced off-line facilitating the recognition of lumen area (inner contour) and media-bounded area (outer contour). + = catheter; calibration = 1mm.

Angiography versus IVUS

To compare angiographic and IVUS qualitative and quantitative data obtained before and after percutaneous transluminal angioplasty (PTA) of the femoropopliteal artery, the records of 135 patients were reviewed.[6] Qualitative and quantitative analysis was performed on corresponding angiographic and IVUS levels. Presence of a lesion and amount of plaque was underestimated angiographically (Fig. 2). In angiographic levels classified as normal, IVUS demonstrated a mean area stenosis of 43%. It was found that angiography had a poor sensitivity for detection of calcified lesions. On angiography a calcified lesion was better detected when the arc of calcification increased in the IVUS cross-sections. A similar relation was found between the detection of dissection seen by angiography following PTA and the extent of dissection seen on IVUS. Overall the incidence of vascular damage seen by IVUS (53%) was higher than seen angiographically (35%).

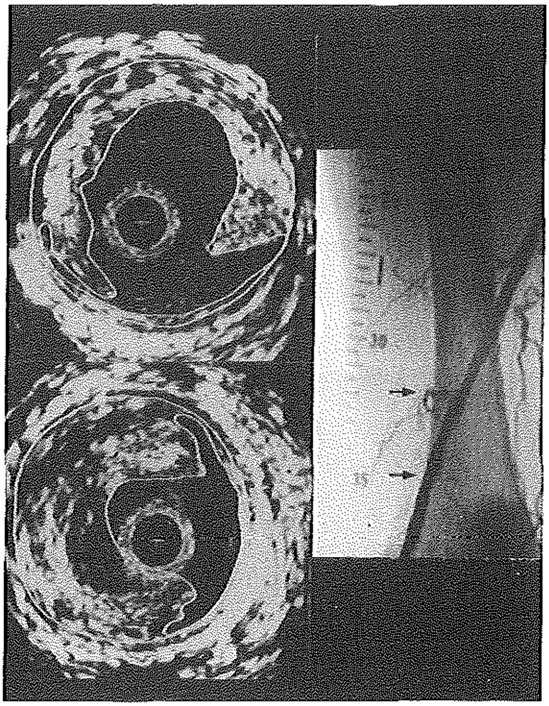

Figure 2. Intravascular ultrasound (IVUS) cross-sections and angiogram obtained from a patient after angiographically defined successful percutaneous transluminal angioplasty (PTA) of the femoropopliteal artery. Note that the presence of a lesion and amount of plaque seen on IVUS is underestimated on the angiogram. The IVUS cross-sections are contour traced off-line facilitating recognition of lumen area (inner contour) and media-bounded area (outer contour). + = catheter; calibration = 1 mm.

Plaque rupture was more frequently seen on IVUS and media rupture was uniquely evidenced by IVUS. Only before PTA there was a good agreement between angiographic diameter stenosis and lumen size seen on IVUS; such a distinct agreement was not seen after PTA.

This finding may be related to the vascular damage after PTA, which allows contrast filling of dissection clefts, distorting the luminal silhouette of the angiogram.

Mechanism of PTA

The basic mechanism of balloon angioplasty described by Dotter and Judkins in 1964 included plaque compression.[7] Based on histologic sections and angiographic records Castaneda-Zuniga et al. proposed that the increase in lumen size is due to media stretch, without significant compression or redistribution of plaque.[8] The introduction of IVUS has enabled the study of the mechanism of balloon angioplasty *in vivo* more precisely. To study the effects of PTA of the femoropopliteal artery with IVUS, corresponding IVUS cross-sections obtained before and after PTA from 115 procedures were analyzed. Vascular damage including plaque rupture, media rupture and dissection was assessed. Lumen area, media bounded area (vessel area) and plaque area were measured (Fig. 3).

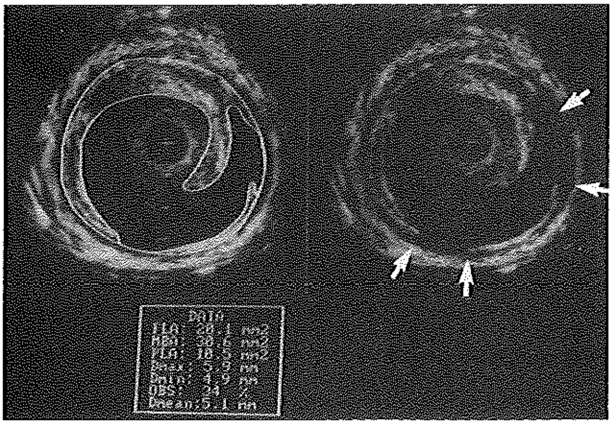

Figure 3. Intravascular ultrasound (IVUS) cross-sections obtained after balloon angioplasty showing media rupture and dissection. Left panel: The IVUS cross-section is contour traced off-line facilitating recognition and measurement of lumen area (FLA), media-bounded area (MBA) and plaque area. (PLA). Right panel: White arrows indicate the sections of media rupture. + = catheter; calibration = 1 mm.

IVUS showed that the increase in vessel area (i.e. media stretch) accounted for 68% of the lumen gain. Over-stretching is accompanied almost always by dissection and plaque rupture and occasionally by media rupture[9] (Fig. 4). The relative contribution of plaque reduction was higher at the target sites, suggesting that the plaque at the target site may be crushed more extensively, leading to redistribution of the plaque material.[10]

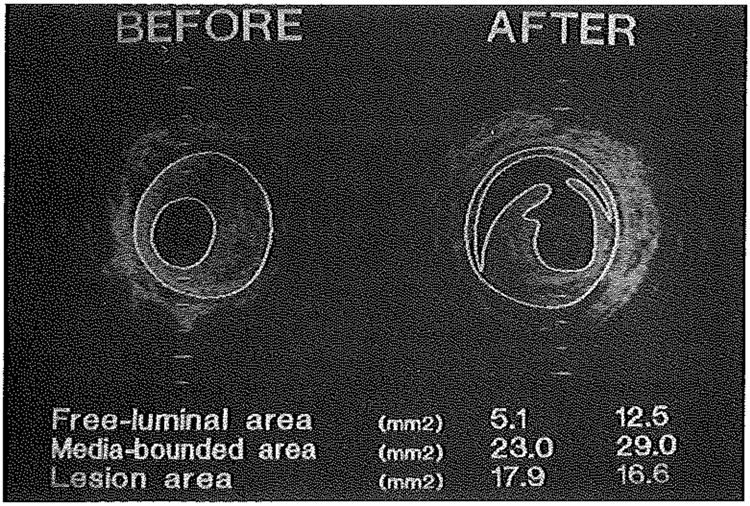

Figure 4. Corresponding intravascular ultrasound (IVUS) cross-sections obtained from a patient before (left panel) and after balloon angioplasty (right panel). The IVUS cross-sections are contour traced off-line facilitating recognition and measurement of lumen area, vessel area and plaque area. Increase in lumen area was associated with significant vessel area increase and minimal plaque area decrease. + = catheter; calibration = 1 mm.

Mechanism of stenting

Stents were developed in order to prevent recoil after PTA and thus improve the immediate and long-term results of balloon angioplasty in different sites. Intravascular ultrasound in coronary arteries has revealed that stents may be incompletely deployed despite optimal angiographic result.[11] Similar lessons concerning stent placement could perhaps be learned in other parts of the vascular system.

For this purpose we performed an IVUS study to compare the balloon diameter with the immediate outcome following stent placement in 22 patients with peripheral obstructive arterial disease. The results show that well-apposed and symmetrically expanded stents as evidenced angiographically, may vary in lumen dimensions despite the use of adequately sized balloons[12] (Fig. 5). A discrepancy was found between the size of the balloon that was used and resulting smallest stent area (difference 31%). Moreover, in 52% of the stents a uniform expansion of the stent was found, in 39% a funnel-like shape (one stent edge larger than the dimension in the mid-portion in the stent) was found, while in 9% of the stents both stent edges were larger than the dimension in the mid-portion of the stent. We postulate that inadequate stent expansion may be caused by either a balloon diameter that is too small for the artery, by compression of the stent by the plaque, or by plaque resistance. The observation that dilatation with both compliant balloons and non-compliant balloons frequently resulted in under-expansion of the stents, suggests that the mechanical properties of the balloon that is used for dilatation and delivery of the stent does not influence the outcome.

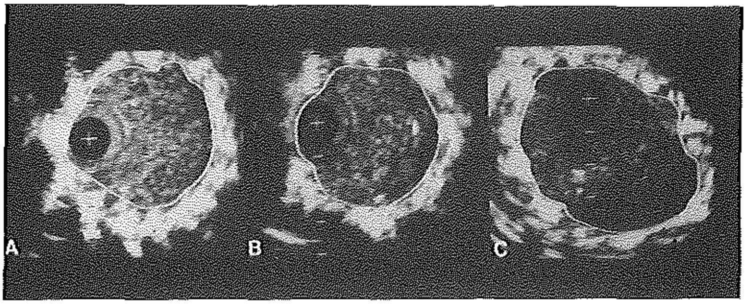

Figure 5. Intravascular ultrasound (IVUS) cross-sections of the femoropopliteal artery in a patient after stent placement for residual stenosis using a 6 mm balloon. The cross-sections are contour traced off-line showing: the proximal stent edge (A), intra-stent (B) and distal stent edge (C) with mean diameters of 4.5 mm, 4.4 mm and 5.3 mm, respectively. + = catheter; calibration = 1 mm.

Mechanism of restenosis

After PTA

Initially, autopsy studies have shown that intimal hyperplasia is responsible for the decrease in arterial lumen after intervention. Later, serial IVUS studies have suggested that vascular shrinkage may be the predominant factor in the development of restenosis.[13] We used IVUS to study the femoropopliteal artery immediately after the initial intervention and at 1 year follow-up. To ensure that IVUS cross-sections obtained after intervention and at follow-up were indeed from corresponding sites, the cross-sections were studied side-by-side and frame-to-frame. The IVUS cross-sections were analyzed for change in lumen area, plaque area and vessel area (media-bounded area). Differences were encountered in the extent of intimal hyperplasia and vascular remodeling at the most stenotic site and in the cross-sections just proximal and distal of the most stenotic site. It was found that the lumen area measured from the corresponding cross-sections decreased significantly both at the most stenotic site (-54%) and in the cross-sections just proximal and distal of the most stenotic site -15%). A significant increase in plaque area was seen both at the most stenotic site (+21%) and in the adjacent cross-sections of the dilated segment (+15%). A significant decrease in vessel area was seen only at the most stenotic site (-9%). The vessel area in the cross-sections adjacent to the dilated segment did not change (1%) (Fig. 6). According to these data, plaque area increase (i.e. intimal hyperplasia) contributed the major part (57%) and vessel area decrease a smaller part (43%) to the lumen area reduction at the most stenotic site.

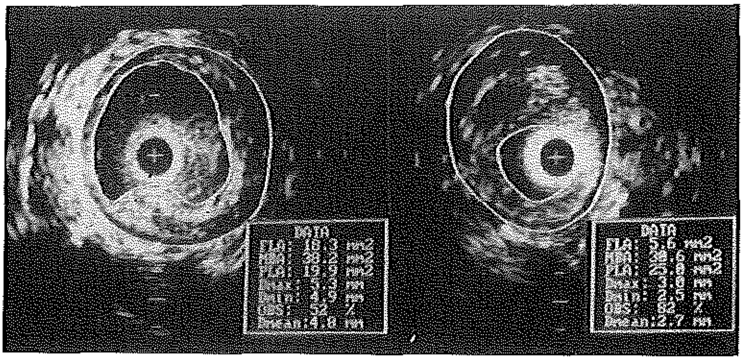

Figure 6. Intravascular ultrasound (IVUS) cross-sections of the femoropopliteal artery in a patient after PTA (left panel) and at 6-months follow-up (right panel). The cross-sections are contour traced off-line facilitating recognition and measurement of lumen area (FLA, inner contour) and media-bounded area (MBA, outer contour). The lumen area (FLA) decreased from 18.3 mm^2 to 5.6 mm^2. The media-bounded area (MBA) decreased from 38.2 mm^2 to 30.6 mm^2. The plaque area increased from 19.9 mm^2 to 25.0 mm^2. + = catheter; calibration = 1 mm.

Furthermore, it was found that in one third of the patients an increase of the vessel area at the most stenotic site was found to compensate for the presence of intimal hyperplasia, which resulted in an unchanged lumen area at follow-up. Similarly, an increase in lumen area was seen in one-fifth of the adjacent cross-sections of the dilated segment due to vessel area increase exceeding plaque area increase. From these observations it can be concluded that in the presence of intimal hyperplasia the type of vascular remodelling (enlargement or shrinkage) determined the net lumen change.

After stent placement

As mentioned above, it has been shown that geometrical arterial remodeling may be the dominant factor contributing to re-stenosis after balloon angioplasty. It is postulated that the use of stents may reduce re-stenosis by eliminating this geometrical remodeling. This assumption is supported by serial IVUS analysis after stent placement in coronary arteries, showing that late recoil of Palmaz-Schatz stents rarely occurred (only in 6% of the cases); and when it did occur, late stent recoil was minimal.[14] The dominant mechanism of late lumen loss was intimal hyperplasia.

We performed a serial IVUS analysis in 2 patients to study the mechanism of re-stenosis after Palmaz stent placement in the femoropopliteal artery.[15] In one patient 7 balloon expandable stents were placed with overlap because of a 22-cm long dissection after PTA of a short but high-grade stenosis. After a good initial success the patient returned 5 months later with recurrent disabling claudication. The angiogram showed distinct stenoses at the stent junctions (Fig.7). IVUS images obtained after stent placement and at follow-up were analyzed for lumen area, stent area, lesion area, and percentage area stenosis. Both intimal hyperplasia (inside the stent) and stent area reduction were common findings responsible for the late lumen loss. An intriguing finding was that the extent of lumen area reduction, intimal hyperplasia and stent area reduction was more severe at the stent junctions. This raised the question whether the amount of metal struts pressing against the arterial wall, or movement of the stent edges, may be responsible for the increased amount of intimal hyperplasia.

In the second patient, IVUS investigation performed 3 years after stent placement for a stenosis in the femoropopliteal artery revealed that a distinct lumen loss was mainly due to stent area reduction. In this stent only minimal intimal hyperplasia was found (Fig. 8). These 2 cases illustrate that, in contrast to coronary artery, remodeling of balloon expandable stents contributes to re-stenosis in the femoropopliteal artery.

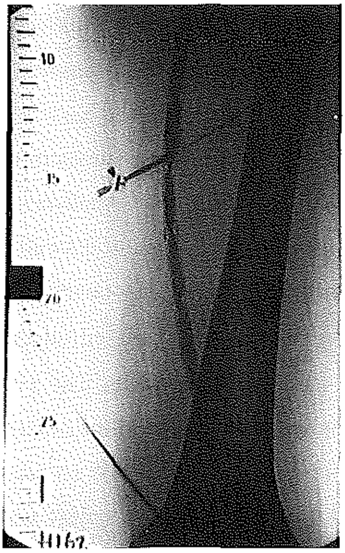

Figure 7. Angiography of the left femoropopliteal artery obtained at 5-months follow-up showing distinct stenoses at the stent junctions.

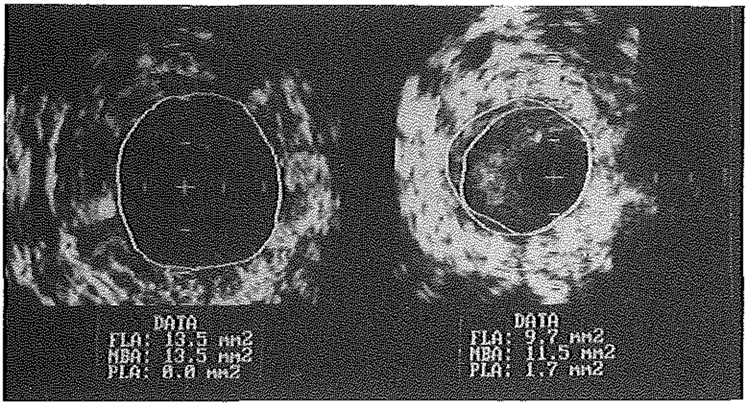

Figure 8. Corresponding intravascular ultrasound (IVUS) cross-sections obtained from a patient after stent placement in the femoropopliteal artery (left panel) and at 3-year follow-up (right panel). The cross-sections are contour traced off-line facilitating recognition and measurement. At follow-up minimal intimal hyperplasia was found (1.7 mm^2).
The stent area (MBA) decrease (from 13.5 mm^2 to 11.5 mm^2) was responsible for lumen area (FLA) reduction.

Intravascular ultrasound predictors of restenosis

In order to determine the additional value of IVUS compared with angiography to predict the outcome following PTA, a multicenter study named EPISODE (Evaluation Peripheral Intravascular Sonography On Dotter Effect) was conducted.[16] The study comprised 39 patients referred for disabling claudication who underwent PTA for femoropopliteal obstructive disease. The intervention was preceded and followed by routine single plane angiography and IVUS investigation. The IVUS parameters selected for analysis included: 1) qualitative and quantitative data obtained at the smallest lumen area before PTA and its matched site after PTA; 2) the mean maximum arc of dissection in the dilated segment; and 3) the presence of dissection and/or media rupture encountered in the dilated segment.

Angiographically, the PTA procedure was classified successful (<50% residual diameter stenosis) in 31 patients and as a failure in 8 patients. The 31 patients were followed to show the duration of success and the time of failure up to the census date of 6 months. Success was scored in 14 of the 31 patients (group 1); failure was scored in 17 patients (group 2). The 8 patients that were angiographically classified as a failure underwent vascular reconstructive surgery.

As result of PTA, a significant increase in lumen area was noted with IVUS both in group 1 and group 2. In addition, after PTA larger values were encountered in the lumen area in group 1 vs. group 2 (6.0 ± 3.6 mm^2 vs. 3.6 ± 2.0 mm^2). Differences were encountered in the extent of hard lesion in group 1 vs. group 2 (12° ± 21° vs. 57° ± 93°). The extent of dissection seen after PTA was significantly less in group 1 vs. group 2 (18° ± 21° vs. 78° ± 69°).

Recently, the EPISODE study was completed with inclusion of a total of 137 patients. Supplementary conclusions are that media rupture in the dilated segments was less frequently seen in procedures with early re-stenosis than early success, but this difference did not reach a statistically significant level. A larger mean arc of hard lesion was an independent predictor of early restenosis.

Clinical implications of the use of IVUS to predict restenosis include:

First, in the presence of an extensive hard lesion (i.e. calcification) in the diseased segment other treatment modalities should be considered after initial failure of PTA.

Second, as the presence of a media rupture is beneficial for the outcome, the absence of vascular damage, especially in the presence of a small lumen area or small luminal gain after PTA, is an indication of an inadequate dilatation and may require a repeat PTA. However, the creation of extensive vascular damage, such as a large dissection, creates a dilemma, as a dissection may be a prerequisite for an adequate dilatation while at the same time this may result in an increased probability for late re-stenosis. Large dissections may necessitate the placement of stents to prevent the late re-stenotic process.

Third, maximizing lumen area, and thus minimizing area stenosis, may reduce re-stenosis. In the presence of a large residual stenosis after PTA, a repeat PTA or stent placement may optimize the result.

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CHAPTER 3

DISCREPANCY BETWEEN STENT DEPLOYMENT AND BALLOON SIZE USED ASSESSED BY INTRAVASCULAR ULTRASOUND

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SUMMARY

Objectives: This study was designed to assess discrepancy in stent deployment seen on intravascular ultrasound and its relation with the balloon size selected for stent delivery.

Design: Retrospective study.

Materials and Methods: The study group comprised 27 patients treated using a stent (n=18) or stent-graft combination (n=9). Following angiographically optimal stent deployment (<10% residual stenosis), intravascular ultrasound was used to compare the smallest intra-stent lumen area with measurements at both stent edges and the lumen area of the proximal and distal reference site.

Results: In 14 of the 27 stents the intra-stent dimension was the same as the dimension of the stent edge (difference ≤+10%). Of the remaining stents the intra-stent dimension was smaller (difference >10%) than the proximal stent edge in three stents (range 11-39%), smaller than the distal stent edge in three stents (range 11-20%) and smaller than both stent edges in three stents (range 12-37%). Both in patients treated with a stent or stent-graft combination, the resulting smallest intra-stent lumen area was smaller than the balloon size used (mean difference32% and 42%, respectively) and smaller than the mean lumen area of the reference sites (mean difference 25% and 23%, respectively).

Conclusions: This intravascular ultrasound study shows a discrepancy between intra-stent lumen area, the area of the stent edges and the balloon size used.

Key words: intravascular ultrasound; stent; diameter; stenosis; aneurysm.

INTRODUCTION

To improve the immediate and long-term results of vascular interventions, stent deployment is used in various vascular sites.[1-3] In the coronary arteries intravascular ultrasound has revealed that stents may be incompletely deployed despite optimal angiographic results and consequently, interventional strategies have been modified.[2,4-8] The present study describes stent deployment in non-coronary sites assessed with intravascular ultrasound, and examines the relationship to the balloon size used.

SUBJECTS AND METHODS

The study included 27 patients (17 men and 10 women, median age 65 (range 36-86) years) successfully treated with a stent (n=18) or a combined stentgraft (n=9) placement. Success was defined as a residual diameter stenosis < 10% with a smooth lumen of the stented segment and without an endoleak to the aneurysm. Balloon-expandable stents were used (Palmaz; Johnson and Johnson, Interventional Systems, NJ, USA).

The subclavian artery (n=4), the common iliac artery (n=10), and the superficial femoral artery (n=13) were treated. Patients were scheduled for intervention based on angiographic data (diameter stenosis >50% or aneurysm). Indications for stenting were suboptimal balloon angioplasty (n=15), elective (n=1), and a dissection larger than the initial lesion (n=2). Stent-graft combinations (Palmaz stent + ePTFE graft) were used to treat peripheral arterial aneurysm (n=6) and false aneurysm at graft anastomoses (n=3).

Dilatations were performed with a compliant balloon (OPTA, Cordis, Europe BV). The size of the balloon and stent were selected on the basis of predeployment intravascular ultrasound. For this purpose the diameter of the original vessel wall (media-to-media) at the location of the diseased stenotic segment was used, or the diameter of the normal lumen where the stent-graft would be anchored. Inflation time and pressure were left to the discretion of the interventionist based on fluoroscopy and angiography

Intravascular ultrasound

Intravascular ultrasound studies were performed with a mechanical system containing a rotating single ultrasound element (30 MHz; Endosonics, Rijswijk, the Netherlands) using a 4.3F flexible catheter ("Princeps"). Before and immediately after intervention the ultrasound catheter was advanced distally and cross-sections were obtained during pullback of the catheter. The resulting images together with their unique frame number were displayed on a monitor via a video-scanned memory and stored on an S-VHS system. Cross-sectional area measurements were performed off-line using a computer-based analysis system[9].

Measurements included 1) *before intervention* assessment of reference vessel area (bounded by the media) in those cross-sections used to determine balloon size and stent size; and 2) *after intervention* assessment of the area at the two stent edges (entry and exit), the smallest area within each stent (intra-stent dimension), and the mean lumen area of the proximal and distal reference segment. The reference segments were by definition within 1-2 cm of the stented segment showing the largest lumen area without sidebranches. Stent deployment was reviewed for:

1) Comparison between the lumen area measured at the deployed stent edges and within each stent. The difference between stent area measured at the edges and within the stent (smallest area) was calculated and expressed as a percentage of the smallest area within the stent. A relative stent area at the stent edge of >110% indicates a larger edge; a relative stent dimension at the edge of 90 to 110% indicates no difference. The cut-off point of 10% was used to correct for intraobserver differences in measurements.
2) Comparison between balloon area and vessel area in those ultrasound cross-sections obtained before intervention on which the size of the balloon used was based. Balloon area was derived from specifications provided by the manufacturer.
3) Comparison between balloon area used and the smallest stent area.
4) Comparison between the smallest stent area and the reference lumen area (mean of proximal and distal reference area) seen after intervention. A distinction was made between data derived from stents and stentgrafts, as well as between data derived from the subclavian, common iliac and femoral arteries.
5) Apposition of the stent to the vessel wall (without protrusion of the struts within the lumen).
6) Stent symmetry at the stent edges and within the stent, which was calculated by dividing minimum and maximum diameter.

To assess intraobserver variability between lumen, vessel and stent areas the cross-sections selected were analyzed by the same observer with an interval of 2 months.

Statistical analysis

All values are given as mean ± standard deviation (SD). Differences in area measurement were examined with the Student's t-test. In order to describe intraobserver agreement the area, mean ± SD of the paired differences between the measurements were given. The Student's t-test was used to determine whether there were systematic intraobserver differences. The degree of intraobserver variation is presented with a coefficient of variation defined as the SD of the paired difference divided by the mean of the absolute value. A p-value <0.05 was considered statistically significant.

RESULTS

The mean length of stents used was 3.0 cm (range 1.0-4.5 cm); the mean pressure to implant the stent against the arterial wall was 11 ± 1 atm.

All intravascular ultrasound studies were completed successfully. Table 1 summarizes the quantitative data obtained.

1) Comparing the intra-stent lumen area and the lumen area of the stent edges individually in each stent, it was found that in 14 stents the areas were in the same order. In the remaining 13 stents either the area of the proximal stent edge (n=7; range 11-39%) or of the distal stent edge (n=3; range 11-20%) was larger than both the intra-stent area and opposite stent edge area (Fig. 1). In 3 stents the intra-stent area was smaller than the area of both stent edges (range 12-37%).

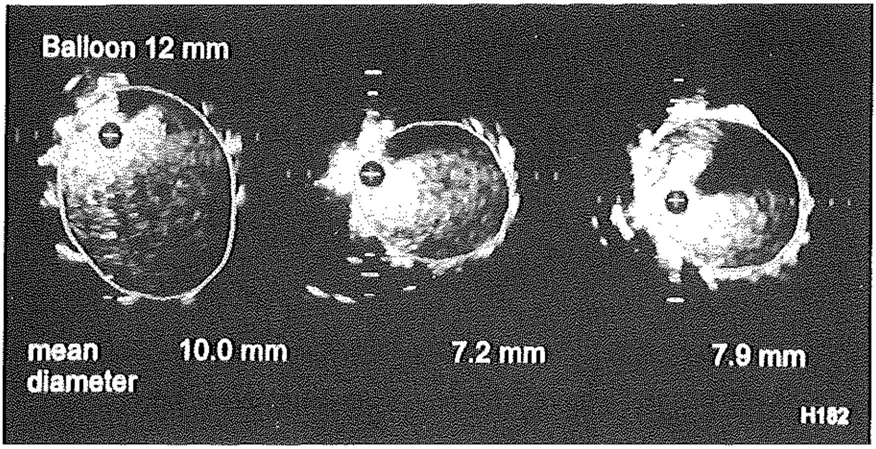

Figure 1. Intravascular ultrasound cross-sections of the iliac artery after stent-graft placement for an aneurysm using a 12 mm balloon. Diameters of the proximal stent edge (A), intra-stent (B) and distal stent edge (C) are smaller than the balloon diameter used. + = catheter; calibration 1 mm.

		Stenosis (n=18) mm^2	Aneurysm (n=9) mm^2
Balloon size		46.8 ± 26.4	93.1 ± 59.6
Before intervention			
Reference vessel area		53.7 ± 31.9	84.4 ± 51.3
After intervention			
Stent area	smallest	32.0 ± 21.4	54.2 ± 35.9
	largest	38.9 ± 24.2	72.4 ± 44.3
Reference lumen area	mean	42.8 ± 29.6	70.8 ± 48.3

Table I. Balloon size and intravascular ultrasound measurements (mean ± SD) through the implanted stent and adjacent vessel segments in the study population.

2) The balloon size selected in patients treated for a stenosis was smaller (13%) than the reference vessel area seen on ultrasound before intervention. In patients treated for an aneurysm the balloon size selected was larger (10%) than the reference vessel area seen on ultrasound.
3) The balloon size used exceeded the resulting intra-stent lumen area. Mean difference between balloon size and smallest intra-stent area was 32% for patients treated for a stenosis and 42% for patients treated for an aneurysm. The difference between the balloon size and smallest intra-stent area was significant for common iliac (44%) and superficial femoral artery (37%), but not for the subclavian artery (11%) (Fig. 2).
4) Comparing the smallest intra-stent area and the lumen area of the reference segment a mean difference of 25% was seen for patients treated with a stent, and 23% for patients treated with a combined stent-graft. Individually, the difference between smallest intra-stent area and reference lumen area was less than 10% in seven patients; between 10% and 20% in three patients and between 20% and 56% in 17 patients.
5) Complete stent apposition with the struts touching the arterial wall was seen in all patients.
6) Data on the symmetry index indicate well-deployed circular stents: an index of ≥0.7 was found in 100% of the stents, and an index of ≥0.8 was found in 95% of the stents, respectively.

Of the intraobserver differences, none were statistically significant. The coefficient of variation of the vessel area assessed before intervention was 5%; for lumen and stent area assessed after intervention it was 7% and 6%, respectively.

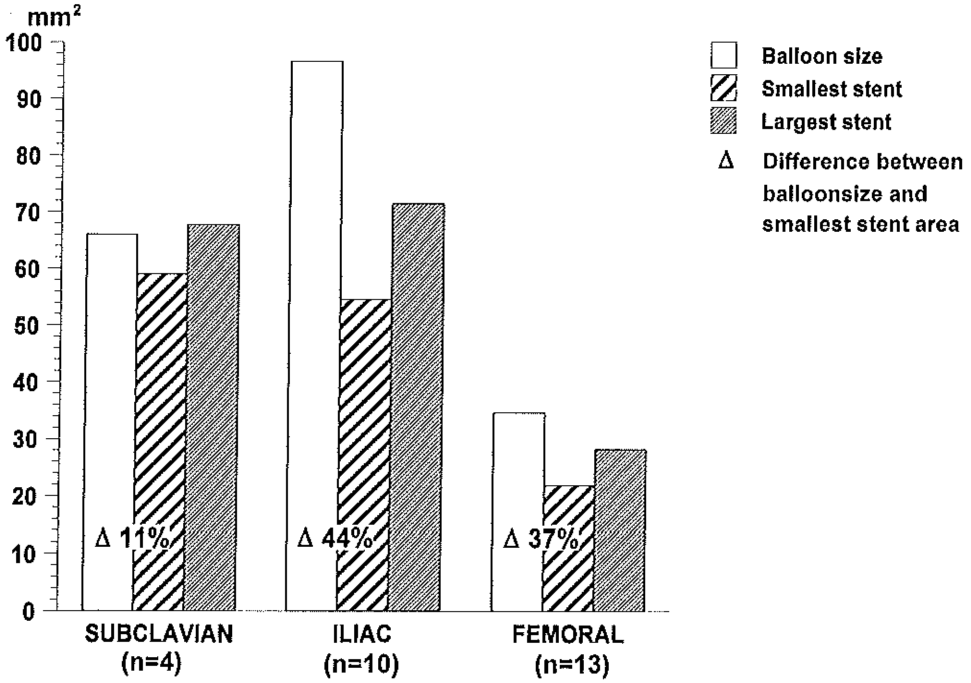

Figure 2. Comparison between balloon size and stent areas measured with intravascular ultrasound. (□) Balloon size; (■) smallest stent; (▒) largest stent; (Δ) difference between balloon size and smallest stent area.

DISCUSSION

Endovascular treatment offers a minimally invasive therapy that is effective in most circulatory beds for an increasing array of pathology[10]. The use of stent and stent-graft combinations to improve long-term patency of endovascular interventions is being investigated[10]. Because angiography alone is insufficient to adequately monitor endovascular procedures, the comprehensive insight into vessel and stent geometry provided by intravascular ultrasound has played an important role in developing the concept of optimized stent deployment[11]. Despite good angiographic appearance the use of intravascular ultrasound in coronary arteries has resulted in a significant increase in intra-stent dimensions[2-4]. Dilatation with low-compliant high-pressure oversized balloon has been advocated[5-8].

The present observational intravascular ultrasound study compared the balloon size used with the immediate outcome following stent or stentgraft implantation. The results show that well-apposed stents can vary in lumen dimensions despite use of adequately sized balloons. As expected, a good agreement was found between balloon size used and the reference vessel area seen prior to intervention. Irrespective of treated pathology, we found that in 14 of 27 stents a uniform expansion of the stent was achieved; a funnel-like shape was observed in 10 stents, while in 3 stents both stent edges were larger than the dimension seen within the stent. Moreover, a discrepancy was observed between balloon area and resulting stent area in patients treated for both a stenosis (difference 32%) and for an aneurysm (difference 42%). If, however diameters were used, the difference between balloon and stent was 18% in patients treated with a stent and 23% in patients treated with a stent-graft combination. These observations concur with others reporting that the balloon diameter used for coronary artery application is larger than the resulting intra-stent diameter (difference 9-25%)[3,4,6-8]. Inadequate stent expansion may be caused by a balloon that is too small for the artery, by compression of the stent by the plaque[3], or by plaque resistance[8]. Because discrepancy in stent expansion in the present study occurred in patients treated for both stenosis and aneurysm, we postulate that inability to expand the stent to a diameter equal to the balloon diameter is due to either the type of balloon used or the nature of the stent. It is noteworthy that in another study we found a similar under-expansion of the stent using a non-compliant balloon (Powerflex, Cordis Europe BV) (unpublished observations). This suggests that the balloon type used may not influence the outcome of stent deployment. It should be mentioned that, in the present study, the angiographic diameter stenosis (<10%) can not be compared with the area stenosis shown by intravascular ultrasound. If ultrasound diameter stenosis for stent and stent-graft combination was calculated, data (12% and 11%, respectively) were in the same order as the angiographic data. The individual differences seen between intra-stent diameter and reference lumen diameter were, however, indicative for a residual stenosis of >10% in 17 patients (between 10-20% stenosis in 11 patients and between 20-33% in six patients). The significance of this finding for clinical outcome is, however, not addressed in this study.

It is noteworthy that only stents in the subclavian artery reached the dimensions of the balloon size used. We assume this to be due to the oblique position of the ultrasound catheter tip within the arterial wall lumen, as such a position results in an elliptic cross-sectional image in which the lumen area appears to be larger than the actual lumen area. This assumption is supported by the finding that the mean minimal intra-stent diameter seen within the subclavian artery stent (7.8 mm) was 13% smaller than the balloon size (9 mm).

Finally, it should be noted that for the present study the nominal size of the balloon was used. However, if its diameter was corrected for the pressure used, the mean expected balloon size increased 11%. This implies an even greater discrepancy between the balloon size used and the resulting intra-stent dimensions.mentioned

Limitation

This study was not designed as an outcome study to test whether these criteria predict clinical results after stent insertion. The study compares the ultrasonically assessed reference vessel area and stent area on the one hand, and the manufacturer's specified balloon diameters on the other. The balloon diameter specified by the manufacturer is determined under *in vitro* conditions. Both vessel wall and obstructing plaque, as well as the stent itself, may influence balloon expansion[9].

CONCLUSION

This intravascular ultrasound study shows a discrepancy between the intra-stent lumen dimensions, the dimension of the stent edges and the balloon size used both in patients treated for a stenosis or an aneurysm. This discrepancy is not seen angiographically. Selection of larger balloon size and/or higher pressures than currently used might be warranted in future clinical applications.

Acknowledgement

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CHAPTER 4

STENT REMODELING CONTRIBUTES TO FEMOROPOPLITEAL ARTERY RESTENOSIS: AN INTRAVASCULAR ULTRASOUND STUDY

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ABSTRACT

This case report describes the status of femoropopliteal artery stents after intervention documented with intravascular ultrasound compared with the changes seen at follow-up. To treat an extensive dissection following balloon angioplasty, a 57-year-old man received 7 adjacent Palmaz stents. At 5 months follow-up angiography and intravascular ultrasound revealed 4 distinct stenotic lesions (≥50%) at stent junctions. Intravascular ultrasound images obtained during the initial stent placement were compared with the corresponding images obtained at follow-up. A distinction was made between changes seen at stent junctions and stent edges (n=8), those seen within each stent (n=7), and those in the non-stented sections proximally and distally (n=3). Intravascular ultrasound established that both intimal hyperplasia and stent area reduction (stent remodeling) resulted in lumen area reduction. The extent of the changes seen at the stent junctions were greater than those seen within the stents: lumen area reduction 67% versus 23%; stent area reduction 26% versus 11%; and intimal hyperplasia 10.8 versus 3.3 mm^2, respectively. Changes in the non-stented sections were minimal (<2%). The stent edge seen at the adductor canal showed elliptical deformation.

Thus, there is a higher risk of restenosis at stent junctions. In addition to intimal hyperplasia, stent remodeling contributes to restenosis.

INTRODUCTION

Stents were developed to improve instant and long-term results of balloon angioplasty. Recently, it has been shown that geometric arterial remodeling (decrease of total arterial cross-sectional area) may be the dominant factor contributing to restenosis following balloon angioplasty[1]. It is assumed that stent may reduce restenosis by eliminating this geometric remodeling[2]. This assumption is supported by serial intravascular ultrasound analysis after stent placement in coronary arteries showing that late recoil of the Palmaz-Schatz stent rarely occurred and, when it did, late stent recoil was minimal. The dominant mechanism of late lumen loss was intimal hyperplasia[3]. The present report describes the changes encountered in the restenosis process following stent placement in the femoropopliteal artery.

CASE REPORT

A 57-year-old man underwent percutaneous transluminal angioplasty (PTA) of the left femoropopliteal artery for treatment of intermittent claudication. Two short, subtotal stenoses (≥90%) in the proximal and distal third of the thigh were dilated using a 6-mm balloon (OPTA, Cordis Europe, Roden, the Netherlands). Because the stenoses persisted an additional PTA was performed. This second procedure was complicated by an extensive 22 cm long dissection evidenced angiographically. It was decided to treat the dissection with Palmaz stents (P394, Johnson & Johnson Interventional Systems, NJ, USA). Following stent placement, intravascular ultrasound was performed using a commercially available mechanical 30 MHz imaging system (Endosonics, Rijswijk, the Netherlands). Details of this system have been described previously[4]. The ultrasound catheter was advanced over a guide wire distally. Under fluoroscopic control, the location of the catheter-tip was compared with a radiopaque ruler. During pull-back, a displacement sensing device was used to document the position of the ultrasound catheter automatically on the video monitor[5]. The images were stored on an S-VHS videotape. For quantitative analysis a digital video analysis system was used[6]. Analysis included measurement of stent area (area within the stent), and stent diameter.

To fix the entire dissection 7 stents were placed with overlap, resulting in a stented segment of 22 cm. Angiography and intravascular ultrasound following stent placement showed a satisfactory result. On intravascular ultrasound the mean stent diameter seen was 5.9 mm (range 4.8 - 6.3 mm). After the procedure the patient was prescribed daily 80 mg aspirin.

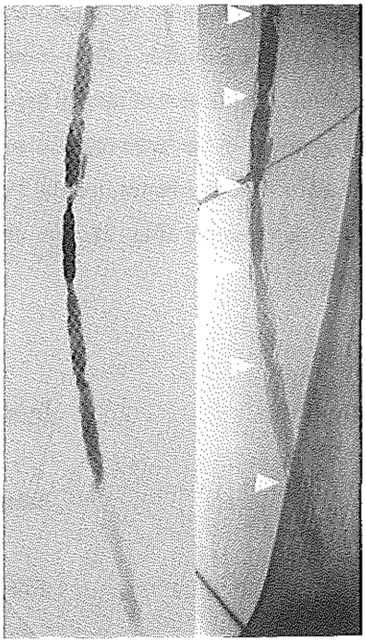

Figure 1. Angiogram of the left superficial femoral artery obtained at 5 months follow-up. Arrowhead = Stent junctions.

Five months after PTA the patient was referred for recurrent symptoms of disabling claudication. Duplex scanning showed multiple stenoses in the stented area. The angiogram showed 4 distinct stenotic sites located at the stent junctions with diameter stenosis of ≥50% (Fig. 1). Intravascular ultrasound was repeated and the images were analyzed for lumen area and diameter, stent area, lesion area, and percentage area stenosis. Lesion area was calculated by subtracting lumen area from stent area. The percentage area stenosis was calculated as lesion area divided by stent area. The stenotic lesions were confirmed by intravascular ultrasound imaging; lumen diameter in these stenoses ranged from 2.5 - 3.1 mm. Segment-to-segment comparisons were made of the intravascular ultrasound images obtained immediately after the first intervention and at 5 months follow-up to reveal the changes that occurred. A distinction was made between measurements at the stent junctions and stent edges ('junctions'), inside the stents ('in-stent'), and in the non-stented reference sections proximally and distally. Quantitative data on lumen area, stent area, lesion area, and percentage area stenosis seen on intravascular ultrasound are listed in Table I. Both intimal hyperplasia (lesion area) and geometric remodeling of the stent (stent area reduction) were common findings responsible for lumen area reduction. The extent of lumen area reduction, intimal hyperplasia, and stent area reduction was more severe at the stent junctions compared with the changes seen inside the stent (Fig. 2). At the most stenotic site seen angiographically, intimal hyperplasia (57%) and stent area reduction (43%) contributed to lumen area reduction evidenced on intravascular ultrasound. The degree of intimal hyperplasia and stent area reduction seen at the most proximal stent edge was in the same order as seen at the stent junctions. At the most distal stent edge, near the adductor canal hiatus, intimal hyperplasia was minimal and the stent showed a distinct elliptical deformation (Fig. 2). The changes seen in the non-stented reference sections were minimal (<2%).

	Junctions (n=8)		In-stent (n=7)	
	mean	**range**	**mean**	**range**
Post intervention				
Stent area (mm²)	26.5	17.9 - 31.1	26.6	21.6 - 28.7
At follow-up				
Lumen area (mm²)	8.8	5.0 - 15.2	20.5	16.5 - 23.1
Stent area (mm²)	19.6	12.4 - 21.6	23.8	19.9 - 27.4
Lesion area (mm²)	10.8	4.7 - 20.2	3.3	0.7 - 6.0
Area stenosis (%)	53	28 - 77	14	3 - 25

n= number of cross-sections.

Table I. Quantitative intravascular ultrasound data obtained from femoropopliteal artery stents immediately after placement and at 5 months follow-up.

DISCUSSION

It is reported that Palmaz stent placement in iliac arteries is a satisfactory alternative to surgery, while placement in the femoropopliteal artery is still controversial[7, 8]. Serial intravascular ultrasound studies have shown that the mechanism related to restenosis, following angiographically successful stent placement in coronary arteries, is progressive intimal hyperplasia[3]. Recently, Khosla et al.[9] investigated the mechanisms of restenosis following renal artery stenting with quantitative angiography. They reported that, in addition to tissue growth, significant stent recoil contributed to the late lumen loss (stent area reduction range 25 - 41%).

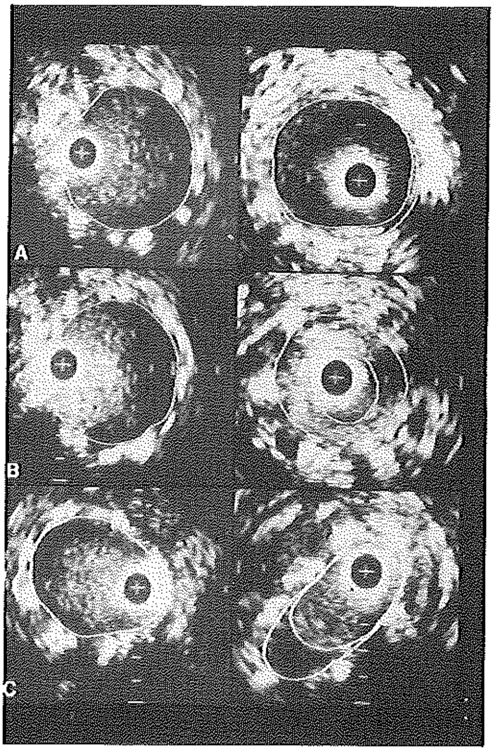

Figure 2. Matched intravascular ultrasound cross-sections of the femoropopliteal artery obtained after stent deployment (left panels) and at 5 months follow-up (right panels). The lumen area (inner contour) and stent area (outer contour) display the quantitative results. A, In-stent changes were minimal. B, Intimal hyperplasia and stent area reduction (remodeling) were the predominant mechanisms responsible for restenosis seen at the stent junctions. C, Distally remodeling of the stent in the region of the adductor canal hiatus. + = catheter; calibration = 1 mm.

The present study revealed, both angiographically and on intravascular ultrasound, that restenosis occurred at the junctions from one stent to the other. On intravascular ultrasound, lumen area reduction was 67% at stent junctions and 23% inside the stents. The mechanisms related to restenosis evidenced with intravascular ultrasound included intimal hyperplasia and stent area reduction. The decrease in stent area was larger at the stent junctions (26%) than seen within the stent (11%). Similarly, the extent of intimal hyperplasia at stent junctions was larger (10.8 mm^2) than that evidenced inside the stent (3.3 mm^2). We assume that stent remodeling may be caused by mechanical forces due to stent articulation at the junctions. The large amount of intimal hyperplasia at the junctions may be explained by the reaction of the vessel wall to these forces. It is noteworthy that changes seen in the non-stented reference sections were minimal. It was found that the stent placed in the vicinity of the adductor canal hiatus showed an elliptical shape at 5 months follow-up. It has been postulated that the femoropopliteal artery undergoes external compression in the region of the adductor canal hiatus[10, 11]. A stent placed at this location may be subjected to external pressure and consequently deform. This observation is validated by an in vitro study showing that Palmaz stents can exhibit permanent plastic deformation under pressure and that the stents may undergo eccentric narrowing[12].

The present study shows that, in addition to intimal hyperplasia, stent remodeling contributes to restenosis. This remodeling consists of a decrease in stent circumference seen at the stent junctions, and elliptical deformation at the adductor canal. This case report provides evidence that there is a higher risk of restenosis at stent junctions. For this reason, one should consider to use one long stent rather than multiple stents for treatment of extensive dissection.

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CHAPTER 5

VASCULAR RESPONSE IN THE FEMOROPOPLITEAL ARTERY AFTER IMPLANTATION OF AN ePTFE BALLOON EXPANDABLE ENDOVASCULAR GRAFT: AN INTRAVASCULAR ULTRASOUND STUDY

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Submitted for publication.

ABSTRACT

Objective: To document vascular dimensions seen after placement of a balloon expandable endograft and the changes at follow-up, using angiography and intravascular ultrasound (IVUS).

Study design: Observational

Subjects and setting: Patients (n=13), treated in the University Hospital Rotterdam with an investigational polytetrafluorethylene endograft for obstructive disease of the femoropopliteal artery, were studied with IVUS immediately after implantation and at follow-up. Corresponding IVUS cross-sections were analyzed for changes in lumen, vessel and plaque area seen in the endograft, in the anastomotic segment and in the remote arterial segment.

Results: The follow-up was completed in 12 patients. The mean follow-up period was 6 (range 1.5-9) months. Matched IVUS cross-sections derived from within the endograft (n=12) and endograft edges (n=23) showed no change in LA in 17, reduction in 11 and dilatation in 7 cross-sections. The LA change in the endograft was minimal (3%) and lesion was absent. Cross-sections obtained at the anastomotic segment revealed no change in LA in 1, a reduction in 4 and a dilatation in 17 cross-sections. LA increase (85%) was associated with an increase in both VA (42%) and PLA (15%). In the remote arterial segment LA showed no change in 6 and a dilatation in 4 cross-sections. The change in LA was minimal (6%), as was the change in VA (9%) and PLA (10%).

Conclusions: Following endograft placement, lumen changes within the endograft, at the endograft edges and at the remote arterial segments were minimal. Intimal hyperplasia was not observed in the endograft. The distinct LA increase involved at the anastomotic segments was determined by the extent of VA and PLA change.

INTRODUCTION

Although percutaneous transluminal angioplasty (PTA) has proven successful in the treatment of focal lesions in atherosclerotic iliac arteries, the long-term results after PTA in femoropopliteal arteries are disappointing given the high incidence of restenosis (1-year patency rates: 47-81%).[1-6] Intravascular ultrasound (IVUS) studies performed in coronary arteries have shown that besides intimal hyperplasia, vascular remodeling (vessel shrinkage) is an important factor in the development of restenosis.[7-9] By eliminating this geometrical remodeling, stents have reduced restenosis in coronary arteries.[10] However, stents used in the femoropopliteal arteries did not improve patency rates. Both intimal hyperplasia and stent area reduction resulted in lumen area reduction, especially at stent edges and stent junctions.[11,12]

To diminish the vascular response to intervention, a polytetrafluorethylene (ePTFE) endograft was developed that covers the damaged arterial wall with an endoprosthesis.

The aim of this study was to assess the vascular response following endovascular graft placement in the femoropopliteal artery with angiography and IVUS.

MATERIAL AND METHODS

Patients

From October 1996 to August 1997, 13 patients with obstructive disease of the femoropopliteal artery were selected to be treated with an endovascular graft. There were 9 men and 4 women, with mean age of 62 (range 47-75) years. Patients were known to have disabling claudication (n=12) or critical ischaemia (n=1). A stenosis (mean length 5.2 cm) was involved in 5 patients and an occlusion (mean length 7.5 cm) in 8 patients. Four patients underwent previous vascular intervention (PTA in 3 and femoropopliteal bypass in 1 patient). The preoperative mean ankle-brachial index was 0.7 in rest and 0.42 after exercise.

Patients were included in the study after giving informed consent for the procedure and the invasive follow-up study.

Endovascular graft

The endograft used is a balloon expandable ePTFE thin-walled graft (ENDURING™, W.L. Gore & Associates, Flagstaff, AZ.) with an outer diameter of 4 mm. The graft wall contains ring-shaped ePTFE reinforcements that are integrated in the material. It can be custom cut in any desired length and, depending on the diameter of the balloon used, the graft can be expanded from 4 to 7 mm inner diameter. This maneuver fixes the graft to the arterial wall over its entire length and provides proper seal. The rings are compression resistant comparable to self-expandable stents.

Operative technique

Procedures were performed in the operation theater under fluoroscopic, angiographic and IVUS guidance. Before insertion of the endograft, a surgical cut-down of the common or superficial femoral artery was performed. In 5 patients with a stenosis and in 5 of 8 patients with an occlusion, a hydrophilic guide-wire was positioned beyond the lesion. Pre-dilatation with a balloon (5-7 mm) was performed to allow passage of a 14 French sheath. In 3 remaining patients with an occlusion, a remote endarterectomy with a MollRing Cutter™ (AneuRx Inc, Cupertino, CA) was performed before a guide-wire was advanced.[13,14] The endograft was cut to the length necessary to cover the entire vessel segment that was pre-dilated or, where a remote endarterectomy was performed, with 1 cm overlap. The endograft was mounted on a dilatation balloon catheter. After insertion of the 14 French sheath in the femoropopliteal artery, the endograft was positioned under fluoroscopic guidance. The sheath was retracted and the endograft expanded. Care was taken that the adjacent arterial segments were not dilated.

Intravascular ultrasound

A 4.3 French motor-driven imaging catheter with a 30 MHz transducer (Endosonics, Rijswijk, the Netherlands) was used. The IVUS transducer was advanced beyond the diseased arterial segment and cross-sectional images were obtained during manual pullback of the catheter. The catheter position was documented using a catheter displacement-sensing device and fluoroscopy, with a radiopaque ruler as reference.[15] Images were stored on an S-VHS videotape.

Follow-up

The follow-up protocol included single plane angiography and IVUS 6 months after intervention. In case of graft occlusion, a control angiogram and IVUS were performed after successful fibrinolysis.

<u>Angiography:</u> The single plane angiograms obtained after placement of the endograft and at follow-up were compared by a radiologist blinded for the IVUS results. By visual inspection the change in the lumen of the endograft and the adjacent arterial segments (i.e. anastomotic segment) and the remote arterial segment (>2 cm) was defined as no change, reduction or

dilatation.

Intravascular ultrasound: IVUS cross-sections obtained after endograft placement and at follow-up were matched using the location derived from the radiopaque ruler and the catheter displacement-sensing device. From each patient the following matched IVUS cross-sections were selected for quantitative analysis: 1) from the *endograft*, the site showing the smallest LA following endograft placement; 2) the proximal and distal *endograft edge*; 3) from the *arterial segment adjacent to the endograft* (i.e. anastomotic segment) cross-sections were selected with an interval of 0.5 cm. From each patient the cross-section showing the largest change in LA in the anastomotic segment was selected and; 4) the cross-section *2 cm remote from this site* was selected for further analysis. Subsequently, the selected cross-sections were digitized and analyzed for lumen area (LA), vessel area (VA) and plaque area (PLA). If no lesion was evidenced in the endograft or at the edges (PLA=0), LA was equal to VA. The matched IVUS cross-sections were grouped according to the change in LA seen at follow-up and classified as: no change (difference <10%), reduction (>10% decrease) or dilatation (>10% increase). Changes in LA, VA and PLA were expressed as median values.

RESULTS

Endovascular graft

The mean length of the endograft used was 20 (range 13-34) cm. The angiogram and IVUS studies from 12 patients were acquired after a mean period of 6 (range 1.5-9) months. In one patient the graft occluded within one week after graft placement as result of a dissection distal to the graft due to sub-intimal graft implantation: follow-up angiogram and IVUS were not available for this patient. In 8 patients the grafts remained patent during the follow-up period (minimally 6 months). In 4 remaining patients acute occlusion of the endograft, encountered at 1.5, 2, 4 and 7 months respectively, was successfully treated with fibrinolysis. In 2 of these patients the graft remained patent. In 2 other patients the grafts re-occluded after 3 and 5 months, respectively.

Angiography

In total, 12 endografts, 20 (8 proximal and 12 distal) anastomotic segments and 10 remote arterial segments were available for analysis. Compared to the implantation angiogram, the angiogram obtained at follow-up showed no change in lumen within the endograft, at the edges of the endograft and in the arterial segments remote from the endograft. Of the 20 anastomotic segments studied, no lumen change was encountered in 9, a reduction in 2 (length < 1cm) and a dilatation in 9 (length <2 cm) segments (Figure 1). No change in lumen was observed in the remote arterial segments.

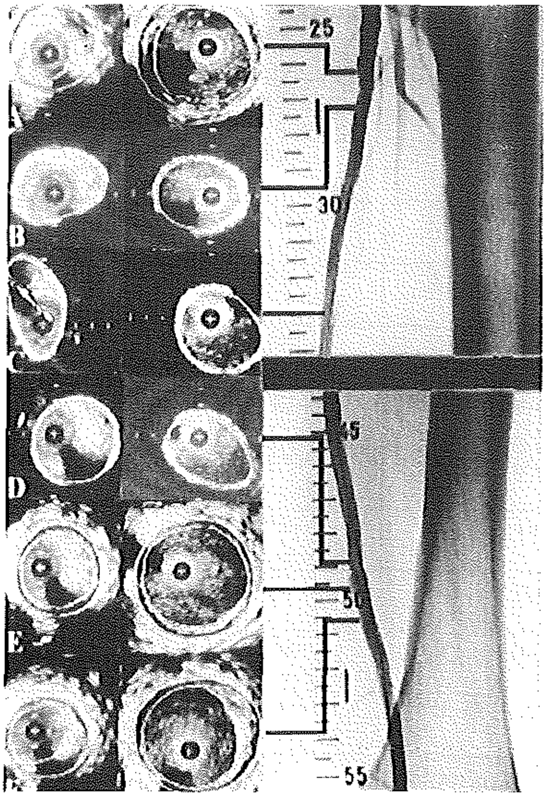


Figure 1. Matched intravascular ultrasound cross-sections of a femoropopliteal artery after endograft placement (left panel) and at follow-up (middle panel) with the corresponding angiogram (right panel). Note absence of plaque inside the endograft. A distinct dilatation seen at the anastomotic segments (A, E, F) is absent in the endograft (B-proximal edge; C-inside endograft; and D-distal edge). Angiography shows a dilatation, but the change is less prominent.

Intravascular ultrasound

Changes seen at follow-up in LA, VA and PLA assessed with IVUS within the endograft, in the anastomotic segments and in the remote arterial segments are summarized in Tables I and II and Figure 2.

	N	LA	VA	PLA
Inside endograft	12	**+3%** (-22% to +45%)	--	--
No lumen change	4	**0%** (-5% to +5%)	--	--
Reduction	3	**-18%** (-22% to –14%)	--	--
Dilatation	5	**+22%** (+12% to +45%)	--	--
Endograft edge	23	**-6%** (-26% to +63%)	--	--
No lumen change	13	**-5%** (-9% to +6%)	--	--
Reduction	8	**-18%** (-26% to –12%)	--	--
Dilatation	2	**+38%** (+13% to +63%)	--	--
Anastomotic segment	22	**+85%** (-56% to +339%)	**+42%** (-16% to +130%)	**+15%** (-11% to + 158%)
No lumen change	1	**+7%**	**+2%**	**-8%**
Reduction	4	**-41%** (-56% to –28%)	**+7%** (-16% to + 27%)	**+69%** (+17% to +156%)
Dilatation	17	**+100%** (+29% to +339%)	**+49%** (+21% to + 130%)	**+13%** (-11% to +158%)
Remote arterial segment	10	**+6%** (-9% to +53%)	**+9%** (-6% to +46%)	**+10%** (-17% to +65%)
No lumen change	6	**+2%** (-9% to +9%)	**+4%** (-6% to +31%)	**+10%** (-3% to +65%)
Reduction	0	--	--	--
Dilatation	4	**+28%** (+13% to +53%)	**+19%** (-3% to +46%)	**+10%** (-17% to +58%)

Bold data represent median changes. N= number of corresponding cross-sections analyzed, LA= lumen area, VA= vessel area, PLA= plaque area, ( ) = range of differences.

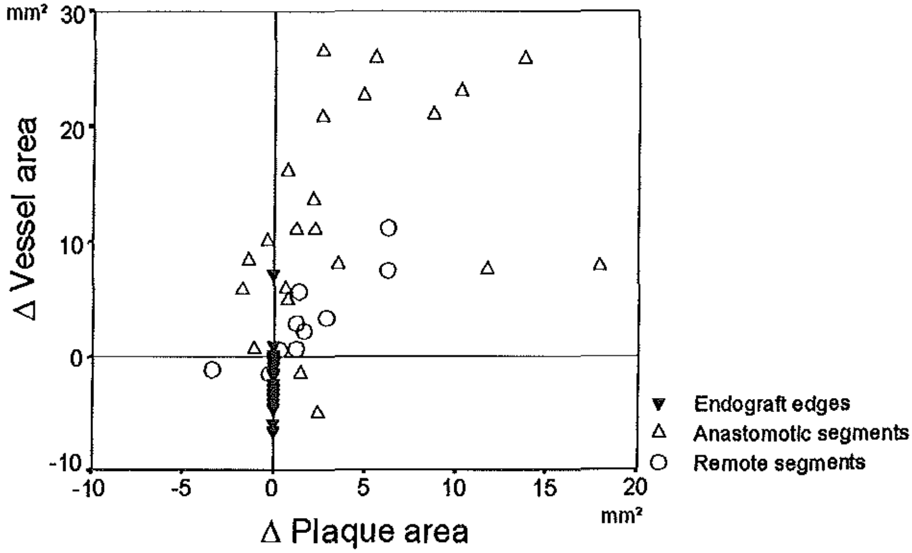
Table I. Changes seen at follow-up in lumen area, vessel area and plaque area assessed with intravascular ultrasound in the endograft, anastomotic segment and remote arterial segment.

	N	LA	VA	PLA
PROXIMAL ENDOGRAFT EDGE (N=11)				
No lumen change	8	**-4%** (-9% to +6%)	--	--
Reduction	2	**-20%** (-26% to –14%)	--	--
Dilatation	1	**+63%**	--	--
DISTAL ENDOGRAFT EDGE (N=12)				
No lumen change	5	**-5%** (-7% to +1%)	--	--
Reduction	6	**-18%** (-22% to –12%)	--	--
Dilatation	1	**+13%**	--	--
PROXIMAL ANASTOMOTIC SEGMENT (N=10)				
No lumen change	1	**+7%**	**+2%**	**-8%**
Reduction	2	**-51%** (-45% to –56%)	**+5%** (-16% to +27%)	**+87%** (+17% to +156%)
Dilatation	7	**+100%** (+75% to +339%)	**+48%** (+32% to +100%)	**+10%** (-10% to +56%)
DISTAL ANASTOMOTIC SEGMENT (N=12)				
No lumen change	0			
Reduction	2	**-33%** (-28% to –38%)	**+7%** (-13% to +27%)	**+69%** (+56% to + 82%)
Dilatation	10	**+90%** (+29% to +188%)	**+54%** (+21% to +130%)	**+18%** (-11% to +158%)

Bold data represents median differences. N= number of cross-sections analyzed, LA= lumen area, VA= vessel area, PLA= plaque area, ( ) = range of differences.

Table II. Changes seen at follow-up in lumen area, vessel area and plaque area assessed with intravascular ultrasound in the endograft edge and the arterial segment adjacent to the endograft.

Endograft: LA change encountered was minimal both inside the endograft (3%) and at the endograft edge (-6%). No lesion was seen within the grafts or at the graft edges (Figure 1). LA showed no change (n=17), a reduction (n=11), or a dilatation (n=7) (Table I). Changes encountered in LA at the proximal and distal endograft edge were comparable (Table II). In one patient the re-occluded endovascular graft was excised after 8 months and histologic examination confirmed the absence of plaque evidenced by IVUS (Figure 3).



Δ Vessel area = changes in mm^2; Δ Plaque area = changes in mm^2.

Figure 2. Remodeling following endograft placement, showing minimal change in the area of the endograft edge and increase in plaque area and vessel area in the majority of the anastomotic segments. At the remote arterial segments the changes are less prominent.

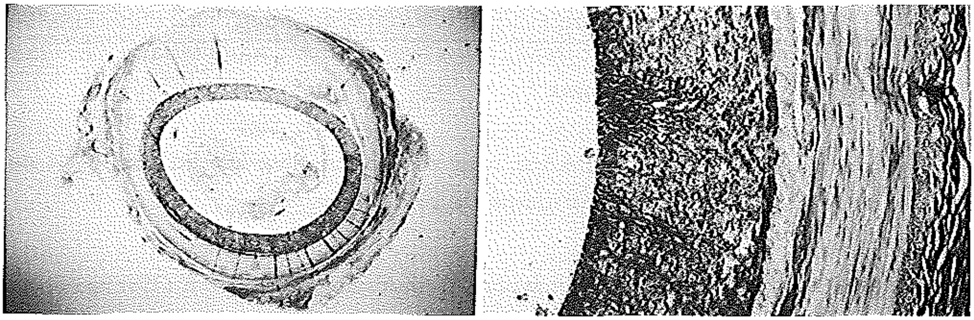


Figure 3. Histology sections (Milligan's Trichrome stain) of an ePTFE endograft in situ (left panel) and its magnification (25X) excised 8 months after endograft placement. No (pseudo) neo-intima is observed within the endograft.

Anastomotic segment: Of the patients studied, 10 proximal and 12 distal anastomotic segment were available for IVUS analysis. The LA increase (85%) was associated with an increase in both VA (42%) and PLA (15%)(Figure 1). The increase in PLA was overcompensated by increase in VA. Individual cross-sections showed no change in LA in 1, a reduction in 4 and a dilatation in 17 cross-sections. No differences were encountered between the proximal and distal anastomotic segment (Table II).

Remote arterial segments: Of the patients studied, 10 remote arterial segments were available for analysis. The minimal change in LA (6%) was associated with an increase in both VA (9%) and PLA (10%). Individual cross-sections showed no change in LA in 6 and a dilatation in 4 other patients.

DISCUSSION

The use of endografts is currently being investigated for both occlusive and aneurysmal disease.[16-21] The present study evaluated a new ePTFE balloon expandable endograft used in patients with obstructive disease of the femoropopliteal artery. At 6 months follow-up the clinical outcome was uneventful in 8 patients, in 5 other patients an acute occlusion of the endograft was observed. Although fibrinolysis was successful in 4 patients, 2 endografts re-occluded after 3 and 5 months, respectively. Due to the limited number of patients evaluated, comparison of primary and secondary patency of the ePTFE endograft and "conventional" PTA or bypass surgery for obstructive disease of the femoropopliteal artery is not yet reliable.

In this study, patients with an endograft were followed with angiography and IVUS. Changes seen at follow-up in the endograft and the remote arterial segments were minimal, both on the angiogram and IVUS. Distinct changes in LA were encountered at the anastomotic segments. The incidence of dilatation seen at the anastomotic segment with IVUS (n=17) was higher than seen with angiography (n=9). This difference might be explained by *visual* judgement of the angiograms as opposed to *quantitative* analysis of the IVUS cross-sections. Moreover, quantitative analysis of the IVUS images enabled to assess the relationship between LA change and the change in VA and PLA.

In this study, the lumen changes seen on IVUS at follow-up both in the endograft (3%) and at the endograft edges (-6%) were minimal. Intimal hyperplasia (PLA increase) and VA reduction (shrinkage), both important parameters in the development of restenosis following PTA, was minimal.[7-9,22] Similarly, the changes in LA in the arterial segments remote from the endograft were minimal (6%) and associated with a minimal increase in VA (9%) and PLA

(10%). These data are in accordance with those reported by van Lankeren et al[22]; in cross-sections not subjected to PTA, LA change (3%) was minimal and associated with an increase both in VA (6%) and PLA (15%).

However, at the anastomotic segments adjacent to the endograft, a distinct LA increase (85%) was associated with a VA increase (42%) and a PLA increase (15%). This finding is remarkable for an arterial segment that is not manipulated by PTA.

Although the mechanism of local dilatation at the anastomotic segment is unclear, there are some hypotheses that may explain the findings.

First: The patency of a prosthetic vascular graft may be determined, in part, by: 1) the healing properties of the graft and 2) by the development of intimal hyperplasia at the anastomotic segment.[23-25] Development of intimal hyperplasia is related to low mean and oscillating shear stress.[26,27] Compared to end-to-side anastomosis, wall shear stress distribution in (endovascular) end-to-end anastomosis may be favorable in preventing turbulent flow, and consequently intimal hyperplasia. Hasson et al[28] described an increase in arterial diameter in a "para-anastomotic hypercompliant" zone distal to end-to-end anastomosis. They suggested that the para-anastomotic hypercompliant zone might be associated with a local high stress induced by compliance mismatch in a direct graft to artery anastomosis.[29-31] This phenomenon may explain our findings related to the increase of LA and VA, but not the increase of PLA.

Second: Dilatation seen at the anastomotic segment at follow-up might be explained by the obstructed flow due to the 14 French delivery sheath used during implantation of the endograft. At follow-up, the angiogram and IVUS were obtained using a 7 French sheath. The higher arterial pressure could be responsible for the increase in.both LA and VA. The fact that this phenomenon was not encountered in the endograft and in the arterial segments remote from the endograft, however, is a counter-argument.

Third: Covering endothelial cells with an endograft may lead to local tissue hypoxia by disconnecting the interaction of blood and the vessel wall. Local tissue ischaemia may lead to the growth of larger arterioles and arteries, including the necessity of remodeling (without sprouting) due to vascular endothelial growth factor ($phVEGF_{165}$).[32] Growth factors or other mediators may play a role in the described findings in this series, although no objective evidence exists.

LIMITATIONS

The main limitation of the present study is the small number of patients available for analysis.

This makes comparison of success rates between treatment of obstructive disease in the femoropopliteal artery by endograft and "conventional" PTA or bypass surgery unreliable. Only 10 remote arterial segments were available for angiographic and IVUS analysis. This was mainly caused by hampered visualization of the proximal remote arterial segment due to the sheath in situ. Another limitation is that the angiogram analysis was performed by visual estimation, whereas the IVUS cross-sections were analyzed quantitatively.

CONCLUSION

Compared to angiography, IVUS is more sensitive in demonstrating changes seen at follow-up. Minimal changes in LA were found within the endograft, at the endograft edges and in the remote arterial segments. Distinct LA increase encountered at the anastomotic segment was associated with an increase in VA and PLA. From the present study, it can be appreciated that vascular remodeling can compensate for intimal hyperplasia at the anastomotic segment of an ePTFE endograft. Endografts may have good application in long segment obstructive disease in the femoropopliteal artery.

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CHAPTER 6

ENDOVASCULAR TREATMENT OF ISOLATED ILIAC ARTERY ANEURYSM

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Isolated iliac artery aneurysm comprise 2-7% of all intra-abdominal aneurysms[1]. The incidence of isolated iliac aneurysm is low, with an estimated prevalence of 0.008-0.1% in large autopsy studies[2]. Combined with abdominal aortic aneurysm the prevalence is 0.65%. The variation of these numbers is caused by the difference in the definition of an iliac artery aneurysm. In some studies an iliac aneurysm is defined as an enlargement of the artery to greater than 1.5 cm in diameter.

Atherosclerosis is the most important aetiological factor in isolated iliac artery aneurysm. Other causes can be infection, surgical trauma, excessive athletic effort (bicycle racing) or collagen diseases, such as Marfan's and Ehlers-Danlos syndrome. Para-anastomotic iliac aneurysms are of totally different aetiology, although operative treatment is the same in most cases. One should consider the possibility of prosthesis disintegration if a para-anastomotic aneurysm is detected in patients with an old, Dacron® bifurcated prosthesis. This is more likely when a double velour Cooley® prosthesis was used. The treatment in these cases is total replacement of the graft.

Reports on the average rates of growth and rupture of these aneurysms are limited, but most authors consider a diameter of 3 cm or more to be an indication for operative treatment.[3] The first successful treatment of an iliac artery aneurysm was described by Valentine Mott in 1927, who ligated a large aneurysm of the common iliac artery. As with abdominal aortic aneurysm, iliac aneurysm can rupture, embolize, thrombose or mimic neurological, urologic and gastro-intestinal symptoms due to external compression.[2,4] In only a minority of the cases one may find a pulsating mass. An aneurysm of the internal iliac artery this can sometimes be felt by rectal examination. Good results are achieved with ultrasound examination, but spiral computed tomography with contrast enhancement is the most effective diagnostic procedure giving exact information on presence, diameter and extension of the aneurysm.

Operative treatment of vessels deep in the pelvis can be of great technical complexity, especially after previous operations. Elective operative treatment is associated with a mortality rate of 7-11%, whereas operative mortality approaches 50% in cases of ruptured iliac aneurysm.[1-3]

Isolated iliac artery aneurysm and para-anastomotic iliac aneurysm can be surgically approached either through a median laparotomy or a retroperitoneal approach. Although supporters of the latter approach claim fewer pulmonary complications and earlier oral food-intake, the choice of approach remains controversial and usually of personal preference. reconstruction. It is safe to open the aneurysmal sac and suture-ligate the branches from the inside to avoid the risk of injury of adjacent structures such as iliac vein, ureter and ischiadic nerve. Control of bleeding in these cases can be achieved with the temporary use of occlusion balloons. An interposition graft can be implanted as an inlay graft in the aneurysm. Exclusion of the aneurysm by ligation alone seems suitable only in cases where there is adequate collateral circulation. In the majority of cases revascularisation by an interposition graft or extra-anatomical revascularisation is mandatory. Both Dacron® and PTFE grafts have been used for surgical reconstruction. In elective cases total ligation of a common or external iliac aneurysm and extra-anatomical revascularisation by means of a femoro-femoral cross-over graft is a satisfactory alternative. In the event of infection an extra-anatomic repair is the treatment of choice.

Proximal ligation only of an isolated internal iliac aneurysm has been claimed to be an adequate and simpler treatment, especially during life-saving operations for other causes and when the internal iliac aneurysm is small. However retrograde filling of the intact aneurysmal sac by collaterals can cause recurrent symptoms in the future.

A more recent and less invasive treatment with reduced operative risk for isolated iliac artery aneurysm involves the use of transluminally placed endovascular grafts.[5-7] The use of stents in combination with a graft offers the possibility to treat focal vascular lesions other than stenosis and occlusion. It is feasible to treat aneurysms, pseudoaneurysms and arteriovenous fistulae in this way. Since August 1995 we have treated 8 isolated and 3 para-anastomotic iliac aneurysms with endovascular stent-grafts. All procedures were performed in the operating theatre by a vascular surgeon and an interventional radiologist. Digital fluoroscopy and intravascular ultrasound (IVUS) were used to navigate the device in position. All stent-grafts were self-made. An ePTFE graft was sewn to a Palmaz stent. Because the size of the introducer sheath (12-16 French) that is required to advance the stent-graft, a surgical cutdown was performed in the common femoral artery in the groin, remote from the site of the aneurysm. Stent-graft delivery and total exclusion of the aneurysm was achieved in 10 of 11 cases. In 1 patient the procedure had to be converted to an open surgical procedure. Because of the tortuosity of the iliac artery it was impossible to position the stent-graft adequately. The duration of the procedure ranged from 2½ to 4½ hours. The mean post-operative hospital stay was 7 days (range 3-18 days). There was no procedure-related morbidity or mortality apart from postoperative fever in one patient. Endovascular stent-grafts are still experimental and have only recently reached clinical application. The major advantage of this procedure is that the aneurysm is treated from a remote site, eliminating the need for extensive intra-abdominal or retroperitoneal dissection. Large side-branches and /or internal iliac artery aneurysm can be coil immobilised intra-operatively. Other potential advantages are the minimal local trauma, rapid postoperative recovery, decreased blood loss and a shorter postoperative hospital stay.

A limited number of published series on endovascular stent-grafts for isolated and para-anastomotic iliac artery aneurysms have demonstrated the feasibility and safety of this technique.[5-8] Long term follow-up in larger series is mandatory to prove the durability of this procedure.

It is expected that in the near future more devices will be commercially available to make this technique easier to perform.[7,8]

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CHAPTER 7

ENDOVASCULAR STENT-GRAFT FOR ANEURYSM OF THE FEMOROPOPLITEAL ARTERY

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Submitted for publication.

ABSTRACT

Objective: To investigate the preliminary use of endovascular stent-grafts for the treatment of aneurysms of the femoropopliteal artery.

Patients and methods: Ten patients with an aneurysm of the femoropopliteal artery referred for endovascular treatment were investigated.

The series consisted a true aneurysm of the superficial femoral artery (n=2), the popliteal artery (n=4), and a Biograft® (n=2) and a false aneurysm of the superficial femoral aneurysm (n=1) and of a composed bypass. In 8 of the 10 patients the stent-graft was composed of a Palmaz stent and ePTFE; in the other two patients a venous covering was used.

The procedure was guided by angiography and intravascular ultrasound (IVUS).

Results: In 8 of the 10 patients the procedure was completed successfully based on angiography and IVUS findings. Three of these patients required an additional intervention, before a satisfactory result was achieved. In 2 patients a conversion to an open surgical procedure was mandatory due to the inability to place the stent-graft in the correct position. In the early postoperative period 2 failures were encountered. During follow-up an occlusion of the stent-graft was found in 1 patient and stenosis of the distal attachment system in another.

Conclusion: Endovascular stent-grafting of aneurysms of the femoropopliteal artery is an experimental technique that should be restricted to a selected group of patients.

Key words: covered stents, endograft, interventional procedure, femoropopliteal artery, IVUS.

INTRODUCTION

Due to the trend in surgery to develop less invasive procedures, the scope of endovascular interventions has continued to expand over the recent years. The use of endovascular stent-grafts is currently being investigated for both occlusive and aneurysmal disease.[1-4] Although these devices are experimental, the procedure has potential advantages. The stent-grafts can be inserted into a remote arterial access site without the need of extensive dissection of the diseased segment.

Of aneurysms of the femoropopliteal artery, the popliteal aneurysm is the most frequent accounting for more than 70% of all peripheral aneurysm.[5-6] Acute thrombosis is the most common complication leading to a limb-threatening situation. Rupture of a popliteal aneurysm is not common.[7] It is suggested that all symptomatic popliteal aneurysms and all other popliteal aneurysms greater than 2 cm in diameter and all those containing thrombus should be managed by elective surgery.[8]

True aneurysms of the femoral artery are rare; false aneurysms usually occur after arterial trauma or infection.

The incidence of aneurysm formation in modified human umbilical vein grafts is reported to be up to 65% in the older grafts; after improvements in processing the graft, the reported incidence is now 17%.[9]

In this paper we report our experience on the use of stent-grafts for peripheral aneurysm guided by angiography and intravascular ultrasound (IVUS).

PATIENTS AND METHODS

Patients

Between August 1995 and April 1997, 10 patients with an aneurysm of the femoropopliteal artery were referred for endovascular treatment.

The series consisted two true aneurysms of the superficial femoral artery (n=2), popliteal aneurysm (n=4), aneurysm in a Biograft® (modified human umbilical vein graft) (n=2), a false aneurysm in a composite bypass (n=1) and a false aneurysm of the superficial femoral artery due to a gunshot wound (n=1).

All patients were men; the mean age was 66 (range 28 - 86) years. In all the cases medical history, physical examination and angiography established the pre-operative diagnosis.

Procedure

Patients were treated in the operating room by a vascular surgeon in cooperation of an interventional radiologist.

Of the 10 stent-grafts used 8 were composed of balloon expandable medium and large Palmaz stents (Johnson & Johnson Interventional Systems, Warren, NJ) and thin-walled polytetrafluorethylene graft (ePTFE)(Gore & Associates, Flagstaff, AZ). The diameter of the ePTFE ranged from 3-4 mm. The Gore-Tex graft is re-enforced with an external Teflon wrap, which can be removed easily to enable dilatation. During deployment of the stent-graft the ePTFE graft can be dilated to 300-400% of its original diameter. The Palmaz stent was sutured to each graft with 2 CV-6 Gore-Tex sutures placed opposite each other. Care was taken that the stent did not stick out the graft, to prevent contact of the bare stent with the vessel wall. In 2 patients a venous graft (greater saphenous vein) was used. Of the 10 intra-operative prepared stent-grafts, 3 stent-grafts were composed of 1 Palmaz stent and a graft covering the entire length of the stent (including the 2 venous grafts) The graft was sewn to the Palmaz stent at its cephalad and caudal end and mounted on a balloon catheter. Two stent-grafts were composed of 2 Palmaz stent sutured at the proximal and distal end of the graft. The length of the graft was 8-cm. resp. 20 cm. The 8-cm long stent-graft was mounted on an 8-cm long balloon. In the case of the 20 cm. long stent-graft the distal stent was dilated first, followed by the rest of the stent-graft. Five stent-grafts were composed of 1 Palmaz stent, sutured at the distal end of a long graft. After insertion of the stent-graft through the sheath, the distal attachment stent was dilated first with a short balloon, followed by dilatation of the entire ePTFE graft in-situ. The proximal end of this stent-graft was finally sutured as an inlay anastomosis at the site of the arteriotomy

Due to the size of the introducer sheath (12-16 French) necessary to advance the stent-graft, a surgical cutdown was performed in the common and superficial femoral artery, remote from the aneurysm.

In all but 2 patients intravascular ultrasound (IVUS) was used together with fluoroscopy.

A 4.3 French mechanically motor-driven, rotating imaging catheter was used with a 1 mm diameter 30 MHz transducer (Endosonics, Rijswijk, The Netherlands). After a guidewire was positioned beyond the aneurysm, an angiogram was performed for roadmapping. The ultrasound catheter was advanced over the guidewire and by slow manual retraction cross-sectional images were obtained. From the IVUS cross-sections, the diameter of the proximal and distal reference segment of the vessel was assessed. The length of the aneurysm was measured both on fluoroscopy and IVUS, using the radiopaque ruler as reference.

After intervention, both control angiogram and IVUS investigation was performed to determine apposition of the stent, total exclusion of the aneurysm, and diameter and configuration of the stent-graft. The procedures were performed under full heparinization (5.000 IE heparin iv.) and patients received anticoagulants postoperatively.

RESULTS

Procedure-related complications

After initial intervention the procedure was judged successful, both on angiography and IVUS, in 5 of the 10 patients. In 5 other patients an additional intervention (n=3) or conversion to an open surgical procedure (n=2) was necessary (Table I).

Patient	Aneurysm	Intra-operative Findings	Surgical Consequences
A	True aneurysm in SFA	Stent-graft too short Ridge in stent-graft	Additional stent-graft Additional stent
B	False aneurysm in a Composed bypass	Tear in native vessel	Additional stent-graft
C	Popliteal aneurysm	Kinking of stent-graft (Fig. 2)	Additional stent
D	Popliteal aneurysm	Inadequate stent-graft position Mural thrombus (Fig. 3)	Conversion
E	Popliteal aneurysm	Impossibility to position stent-graft	Conversion

SFA= superficial femoral artery

Table I. Clinical data on patients in whom an additional intervention or conversion to an open surgical technique was mandatory.

Patient A with an aneurysm of the superficial femoral artery was treated with an 8-cm long stent-graft composed of thin-walled ePTFE and 2 Palmaz stents (P308). The stent-graft was mounted on a 12 mm., 8 cm long Cordis Opta balloon (Cordis Europe, Roden, the Netherlands). After implantation, angiography and IVUS investigation revealed a proximal leakage due to a too short stent-graft and a stenosis within the graft due to ridge of the ePTFE; foreshortening of the stent-graft caused the latter. During dilatation, the "dog-bone" shape of the dilatation balloon forced the two stents at the ends of the graft towards each other. It was decided to coverseal the leakage with an extra stent-graft and to treat the stenosis with an additional stent and. After these additional interventions both the completion angiogram and IVUS confirmed a satisfactory result.

<u>Patient B</u> had a composite femoro-crural bypass 7 years previously. He was submitted to the hospital with a swelling in the left thigh. A contrast enhanced spiral CT showed a false aneurysm at the anastomosis of the ePTFE and the vein part of the bypass. Because of the aneurysm the bypass was compressed and angulated (Fig. 1). The stent-graft used was composed of a Palmaz stent (P394) and venous covering. The 4-cm long stent-graft was delivered on a 6-mm balloon. Because the sheath could not pass the angulation, it was decided to advance the bare stent-graft through the angulation. During this procedure the struts of the stent torn the bypass and a new stent-graft was implanted successful to coverseal the leakage.

<u>Patient C</u> had a popliteal aneurysm, which was treated with a 20-cm long stent-graft, composed of an ePTFE graft and 2 Palmaz stents (P308). The stent-graft was delivered on a 10–mm balloon. After intervention, the stent-graft showed kinking at the level just above the aneurysm, caused by severe coiling of the vessel (Fig. 2). A 4-cm long Palmaz stent (P394) was implanted at the level of the kinking and completion angiography showed a satisfactory result.

<u>Patient D</u> had a popliteal aneurysm that was treated by an endovascular bypass, composed of an ePTFE graft and a Palmaz stent (P294). The distal stent was positioned in the infra-genicular popliteal artery and dilated with a 8-mm balloon. During dilatation of the ePTFE slight tension was administered to the bypass. Under fluoroscopy it was seen that the distal attachment system had dislodged. After revision of the IVUS data it was observed that the shape of the popliteal artery was more conical than expected from angiography (Fig. 3). The procedure was aborted and an in situ femoropopliteal bypass was performed.

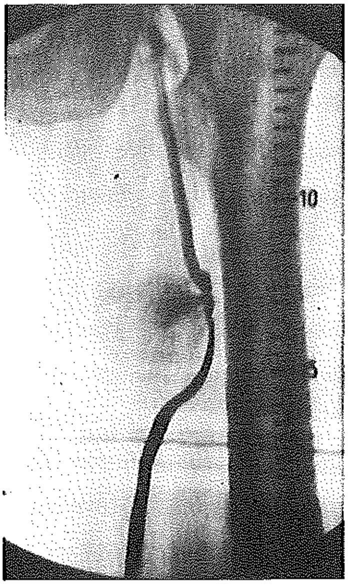

Figure 1. Angiography showing compression and angulation of the composed bypass due to the aneurysm.

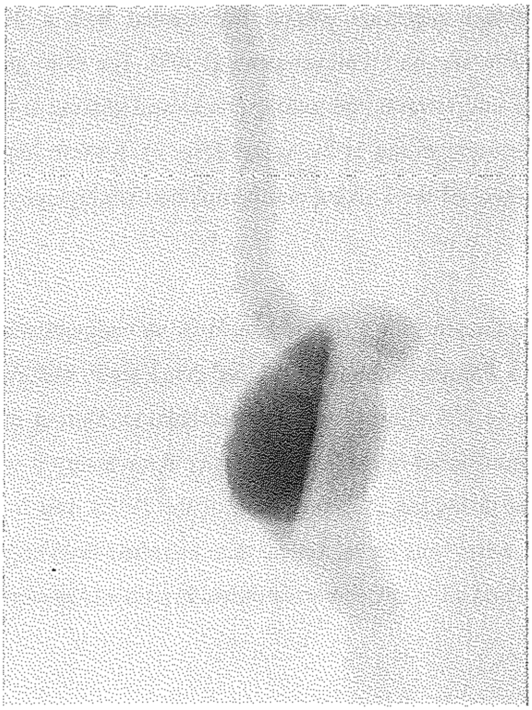

Figure 2. Angiography showing severe coiling of the femoropopliteal artery just proximal of the aneurysm.

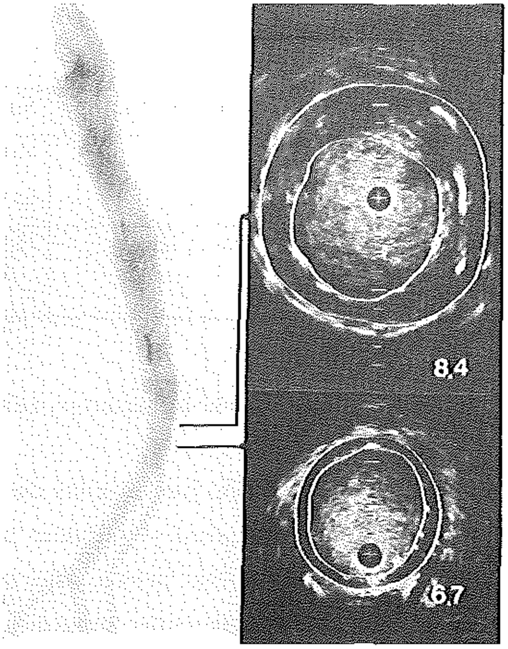

Figure 3. Left panel: angiography. Right panel: Intravascular ultrasound (IVUS) cross-sections. On the IVUS cross-section is seen that the popliteal artery is more conical than expected on the angiography. In the upper IVUS cross-section the mean diameter of the lumen is 8.4 mm, in the lower 6.7 mm. Mural thrombus is not demonstrated on angiography.

Patient E had a popliteal aneurysm. The stent-graft used was composed of an ePTFE graft and a Palmaz stent (P294). Because it proved impossible to advance the stent-graft to the correct position due to the coiling of the popliteal artery, the intervention was converted to an open surgical procedure.

Post-operative complications

In the direct post-operative period 2 patients had complications which made a re-intervention mandatory and a bypass was implanted (Table II).

Patient C is the above-mentioned patient with the kinking of the stent-graft due to severe coiling of the vessel, treated with an additional stent. One day after intervention the stent-graft was occluded. After fibrinolysis a new kinking was seen just above the last implanted Palmaz stent. A long Wallstent (Schneider Inc. Minneapolis, MN) was implanted to straighten the kinking. One day later the bypass occluded again and an in situ venous bypass was performed.

Patient	Aneurysm	Post-operative complication	Surgical consequence
C	Popliteal aneurysm	Acute occlusion	Extra stent In situ venous bypass
F	False aneurysm of SFA	Leakage due to tear in venous Covering (Fig. 4)	In situ venous bypass

SFA = superficial femoral artery

Table II. Clinical data on patients in whom a re-intervention was mandatory in the direct post-operative period.

Patient F had a false aneurysm of the superficial femoral artery due to gunshot wound. The aneurysm was treated with a stent-graft composed of a Palmaz stent (P394) and venous covering. The stent-graft was delivered on a 6-mm balloon. After intervention, angiography showed total exclusion of the aneurysm. Two days after intervention, the patient had severe bleeding from the gunshot wound. At exploration a persistent leak was found at the site of the false aneurysm. The stent-graft was removed and a tear was seen in the venous covering caused by the dilatation (Fig. 4). An in situ venous bypass was performed.

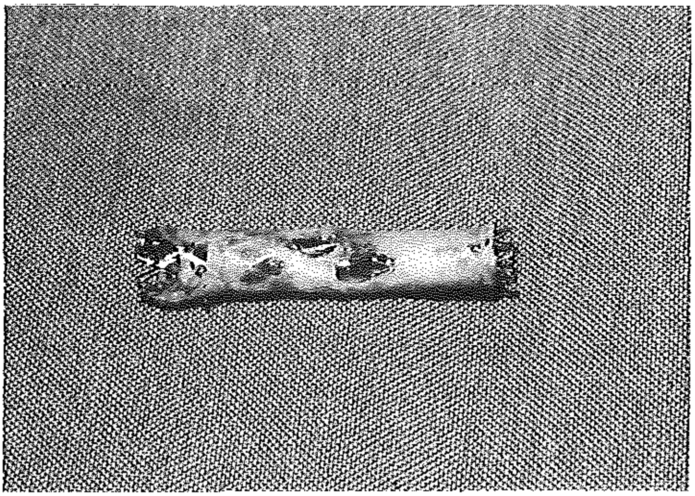

Figure 4. Stent-graft with venous covering. Tears in the covering caused by dilatation.

Follow-up

A summary of the clinical data and follow-up is given in Table III. The mean follow-up of the

6 remaining stent-grafts was 16 (range 6 - 24) months. In 4 of the 6 patients the follow-up was uneventful. A duplex investigation was performed every 6 months.

In one patient a malignancy of the lung was diagnosed 2 months after the patient had received an endovascular bypass for an aneurysmatic Biograft® prosthesis. A lobectomy was performed. At follow-up the stent-graft had occluded after 6 months, but without significant symptoms.

Another patient had an successful endovascular stent-graft for an aneurysmatic Biograft® prosthesis. After 5 months the patient was referred for severe intermittent claudication. Duplex investigation and angiography showed a severe stenosis at the distal stent. IVUS showed intimal hyperplasia at the distal stent edge (Fig. 5). A balloon angioplasty of the distal stent and the popliteal artery was performed.

Patients	Aneurysm	Length Stent-graft	Number of Stents used	Additional procedure	Follow-up
A	Aneurysm SFA	8 cm	2 (P308)	Additional stent-graft Additional stent	Uneventful
B	False aneurysm composite bypass	4 cm	1 (P394)	Additional stent-graft	Uneventful
C	Popliteal aneurysm	20 cm	2 (P308)	Additional stent	Early occlusion due to kinking
D	Popliteal aneurysm	±40 cm	1 (P294)	Conversion	
E	Popliteal aneurysm	±40 cm	1 (P294)	Conversion	
F	False aneurysm SFA	4 cm	1 (P394)		Early conversion due to leakage
G	Aneurysm in Biograft	7 cm	2 (P394)		Occlusion at 6 months
H	Aneurysm in Biograft	30 cm	1 (P394)		Stenosis at distal attachment
I	Popliteal aneurysm	±40 cm	1 (P204)		Uneventful
J	Aneurysm in SFA	4 cm	1 (P394)		Uneventful

SFA=superficial femoral artery

Table III. Clinical data on all patients.

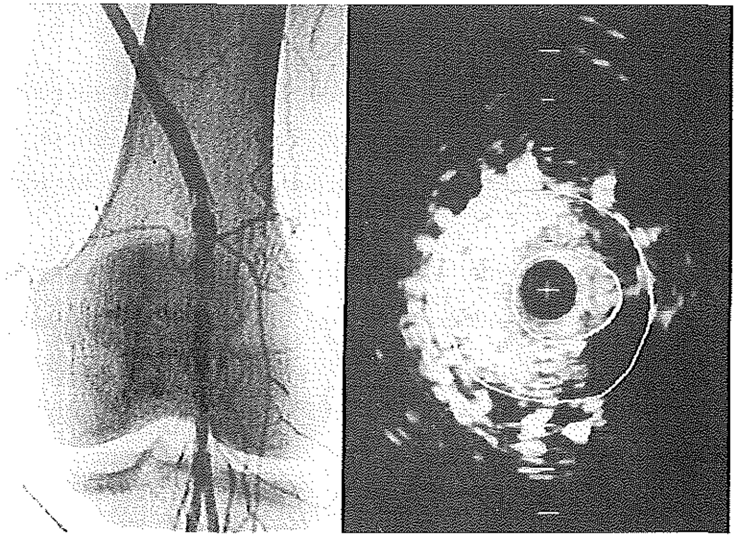

Figure 5. Left panel: angiography. Right panel: Intravascular ultrasound (IVUS) cross-section. Angiography of an endovascular stent-graft showing a stenosis at the distal attachment system. In the IVUS cross-section is seen that the stenosis is caused by intimal hyperplasia.

DISCUSSION

In recent years there is a growing interest to treat several types of vascular lesion with endovascular stent-grafts. Endovascular stent-grafts have been used successfully to treat aortic and peripheral aneurysms, vascular trauma and stenotic or occlusive arterial disease.

One of the drawbacks after endovascular intervention for occlusive disease is re-stenosis, a problem not expected with covered stents in aneurysmatic disorders.

There are numerous reports on endovascular treatment of abdominal aortic aneurysm and the problem of endoleaks is often addressed.

In our institution we have used endovascular stent-grafts for isolated iliac aneurysm with satisfactory results[10] ; these results are comparable to those reported by others.[11]

The problems associated with endovascular treatment of aneurysm of the femoropopliteal artery seem to be of a different nature; there are few reports on this procedure, and the numbers of patients in these reports are limited.[1-3]

Imaging pre-operatively and during the endovascular intervention is of eminent importance. Although angiography, CT scanning and magnetic resonance angiography play an important role in the pre-operative assessment of vascular disease, these modalities do not always provide accurate information on the diameter of the vessel and the extent of the disease. This is clearly demonstrated in patient D, in whom the angiography underestimated the diameter of the diseased segment and did not demonstrate the mural thrombus.

In the present study intra-operative IVUS was used to assess and to measure the diameter of the proximal and distal reference segment of the vessel and the length of the aneurysm, using the radiopaque ruler as reference. Based on these data the balloon size and the diameter and length of the stent-graft were determined. After intervention, a control angiogram was performed, followed by IVUS examination. Apposition and diameter of the stent, exclusion of the aneurysm and configuration of the stent-graft were determined. The IVUS investigation provided additional information that enabled us to optimize the procedure based on better understanding of the extent of the disease and of the encountered problems following intervention.

In our experience endovascular treatment of aneurysm of the femoropopliteal tract is more complex than the treatment of iliac aneurysm. Due to the greater distance manipulation of devices and exact positioning of the stent-grafts can be more difficult. Besides that, the benefits of the minimally invasive aspect of the endovascular procedures are larger for the treatment of the more centrally located aneurysms.

The search for an ideal endovascular stent-graft has produced combinations of several stents (Palmaz, Cragg and Gianturco) with several coverings (ePTFE, Dacron, polyester and autologous vein). In the current series we chose for ePTFE because of its biocompatibility, durability, expansibility and commercial availability.[12, 13] In 2 patients a venous covering of the stent was used; for the patient with the gunshot wound a venous covered stent was considered to reduce the risk of infection. The disadvantage of using a vein for covering is that little is known about expansibility. In this study a tear in the venous covering was caused by dilatation in one patient (F). In addition, previous punctures in the vein, or phlebitis, may reduce the elastic properties of the covering.

During follow-up, occlusion may occur due to stenosis at the stent edges. In the present series a stenosis was seen at the distal edge of the stent-graft in one patient, which was treated by balloon dilatation. The cause was intimal hyperplasia through the struts of the bare segment of the stent. It is therefore advised to entirely cover the stent with the ePTFE and to achieve a good apposition between the stent and the graft. Moreover, during dilatation of the stent-graft care should be taken that the "dog-bone effect" does not cause sliding of the graft of the stent. Another cause of (re-)stenosis may be remodelling of the stent.[14] This was not encountered in this study.

CONCLUSION

Endovascular stent-grafting is an experimental technique that can be performed at different sites of the vascular bed. Although we realise that the numbers presented in this series are limited and that some of the encountered problems are due to a learningcurve we opine that stent-grafts for peripheral aneurysm of the femoropopliteal tract should be only used in a selected group of patients. IVUS enabled us to optimize the procedure based on better understanding of the nature of the underlying disorders. It is expected that more devices will soon become commercially available to make this technique easier to perform. However, well-designed studies are needed to demonstrate their safety and efficacy and show that this technique is superior to the standard treatment.

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CHAPTER 8

INTRAVASCULAR ULTRASOUND IN ENDOVASCULAR STENT-GRAFTS FOR PERIPHERAL ANEURYSMS: A CLINICAL STUDY

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ABSTRACT

Purpose: To evaluate the potential diagnostic information of intraprocedural intravascular ultrasound (IVUS) in patients undergoing endovascular stent-graft for peripheral aneurysm.

Methods: IVUS was used in 17 patients before the intervention to assess the diameter of the proximal and distal neck and the length of the aneurysm. Balloon diameter and stent-graft sizes were selected based on these measurements. Following stent-graft deployment, angiography and IVUS were used to document stent apposition and the configuration and diameter of the stent-graft.

Results: Stent-graft insertion was considered successful in 8 patients based on angiography and IVUS images. In 9 others, both imaging modalities showed inadequate results, necessitating 12 additional procedures: Balloon angioplasty for stent-graft stenosis (2) and inadequate stent-graft apposition (1); an additional stent-graft (4); an extra stent (1); thrombectomy (2); and conversion (2) for inadequate stent-graft position and a graft rupture. In these patients, intraprocedural IVUS was superior to angiography in contributing vital information to aid in the selection of the additional interventions.

Conclusions: During management of peripheral aneurysms with endovascular stent-grafts IVUS monitoring was a useful adjunct when the initial procedure was unsatisfactory and/or when intraprocedural angiographic studies were not conclusive.

Key-words: endovascular grafting, procedural assessment, imaging, Palmaz stent, polytetrafluoroethylene

INTRODUCTION

In recent years, the proliferation of percutaneous endovascular techniques has spawned the development of many new intraluminal devices. Among these, intravascular ultrasound (IVUS) is one of the more promising assessment tools because it provides histology-like high resolution cross-sectional images of the artery. This feature, coupled with the more recent advent of three-dimensional (3D) image reconstruction, has made IVUS especially useful in describing morphological characteristics of the vessel wall in conjunction with interventional techniques.[1-6]
The major goals in the treatment of peripheral vascular obstructive disease are to improve primary results in order to reduce complications, lessen restenosis and prolong long-term patency. With this in mind, we began to investigate the role of IVUS in endovascular stent-grafting of peripheral aneurysms. In this report, we evaluate the contribution of intraoperative IVUS-derived information to the procedure and treatment plan.

METHODS

Between August 1995 and December 1996, 17 patients (16 males; mean age 66 years, range 28 to 86) were referred for endograft treatment of peripheral aneurysms: 11 iliac , 5 femoropopliteal, and 1 celiac axis. In all cases, the preoperative diagnosis was established by medical history, physical examination, angiography and spiral computed tomography (CT) .
Informed consent for the endograft procedure was obtained from all patients after explanation of the risks, benefits, and alternative therapies.

IVUS Apparatus and Endograft Construction

For intraprocedural IVUS imaging, a 5F, mechanically motor-driven, rotating, imaging catheter (Endosonics, Rijswijk, The Netherlands) with a 1 mm diameter 30 MHz transducer was used. The axial resolution of the system was more than 225 μm at a depth of 1 mm. The images were displayed on a monitor by means of a video-scanned memory of 512x512 pixels with 256 shades of grey. Markers were displayed for calibration purposes. The ultrasound images were recorded on S-VHS videotape together with the calibration markers for review and analysis.
All but one of the stent-grafts were composed of Palmaz stents (Cordis Endovascular, a Johnson & Johnson Co., Warren, NJ, USA) covered externally with a thin-walled polytetrafluoroethylene (ePTFE) tube graft (WL Gore & Associates, Flagstaff, AZ, USA).[7-11]
The ePTFE material ranged in diameter from 3 to 6 mm but was expanded to 300% to 400% of its original diameter during deployment. In one case, a venous graft (greater saphenous vein) was used as the stent covering.[12] Each graft was sewn to the stent at the cephalad and caudal ends.

The stent-grafts were manually placed over a compliant balloon (Cordis Europe, Roden, the Netherlands) with a diameter ranging from 6 to 15 mm.

Endograft Procedure

Patients were treated in the operating room by a vascular surgeon and an interventional radiologist. Due to of the size of the stent-graft sheath (12F to16F), a surgical cutdown was performed at the remote access artery (common femoral [n=16] or brachial [n=1]).

A 7F introducer sheath was placed, and a 0.035-inch hydrophilic guidewire was positioned under fluoroscopic guidance beyond the aneurysm. Following the initial roadmapping angiogram, the ultrasound catheter was introduced over the guidewire and advanced beyond the lesion Cross-sectional images were obtained by slow manual retraction of the catheter. The position of the catheter tip was recorded under fluoroscopy with the use of a radiopaque ruler. The diameters of the proximal and distal "normal" reference vessel were acquired from the IVUS images, but the length of the aneurysm was measured using the radiopaque ruler as reference. The balloon size and the diameter and length of the stent-graft were determined from these data.

Subsequently, the 7F introducer sheath was exchanged for the larger 12F to16F sheath. The selected stent-graft was positioned under fluoroscopic guidance and dilated with a compliant balloon (OPTA, Cordis Europe,). After intervention, a control angiogram was performed, followed by IVUS examination to assess stent apposition, exclusion of the aneurysm and the diameter and configuration of the stent-graft. Ultrasound recordings were marked online during the procedure and reviewed for later quantitative analysis.

RESULTS

In this study no adverse effects attributable to intra-operative IVUS were observed. Before intervention, IVUS revealed an unexpected stenosis of the access artery in 2 patients (one in the iliac artery and one in the femoral artery). Both required pre-dilatation before the larger sheath could be advanced.

After intervention, the initial procedure was deemed successful in 8 patients based on angiographic and IVUS parameters. In these cases, IVUS showed total exclusion of the aneurysm, good apposition of the stent-graft to the “normal” arterial wall both cephalad and caudal of the aneurysm, no irregularities inside the stent-graft and no damage to the vessel wall. In 9 other patients, however, one or more additional procedures (total 12) were deemed mandatory based on the procedural assessment data derived from intra-operative IVUS imaging (Table 1).

Patient	Location of aneurysm	Intra-operative findings	Surgical consequences
A	Iliac	Stenosis in stent-graft Thrombus	Additional balloon angioplasty Thrombectomy
B	Iliac	Stenosis in stent-graft	Additional balloon angioplasty
C	Iliac	Inadequate stent-graft apposition Thrombus	Additional balloon angioplasty Thrombectomy
D	Iliac	Stent-graft too short	Additional stent-graft
E	Iliac	Inadequate stent position Rupture graft	Conversion
F	Femoral	Stent-graft too short Ridge in stent-graft	Additional stent-graft Additional stent
G	Femoral	Tear in native vessel	Additional stent-graft
H	Femoral	Inadequate stent-graft position	Conversion
I	Coeliac	Stent-graft too short	Additional stent-graft

Table I. Data on patients (n=9) in whom intra-operative intravascular ultrasound follwing intervention revealed significant information

In 2 patients, conversion to an open surgical procedure was necessary; both had improperly positioned stent-grafts, but one also showed rupture of the graft. Additional balloon angioplasty was performed in 3 patients: 2 for stenosis in the endograft and the third for inadequate device apposition to the wall. An additional stent-graft was inserted in 4 patients, 3 owing to deployment of a too-short device, and the fourth due to a tear in the native vessel wall. A stent was used in 1 patient to correct a lumen-narrowing ridge that had developed in the endograft. The finding of thrombus in the treated segment prompted thrombectomy in 2 patients. Following these additional interventions, the procedures were judged successful by angiography and IVUS in all patients. In the cases where a stenosis was detected, the mean diameter of the stent-graft increased 69% (range 18-100%).

The importance of the IVUS findings is illustrated most effectively by three cases in particular. Patient 3, who received a bifurcated aortoiliac Dacron graft in 1986, was referred for repair of a false aneurysm of the iliac artery. After the stent-graft was positioned, the angiogram showed a stenosis at the distal stent and an endoleak. IVUS examination revealed inadequate stent-graft apposition, making further dilatation necessary. In addition, a thrombus was seen on IVUS, thrombectomy effectively alleviated the problem (Fig.1).

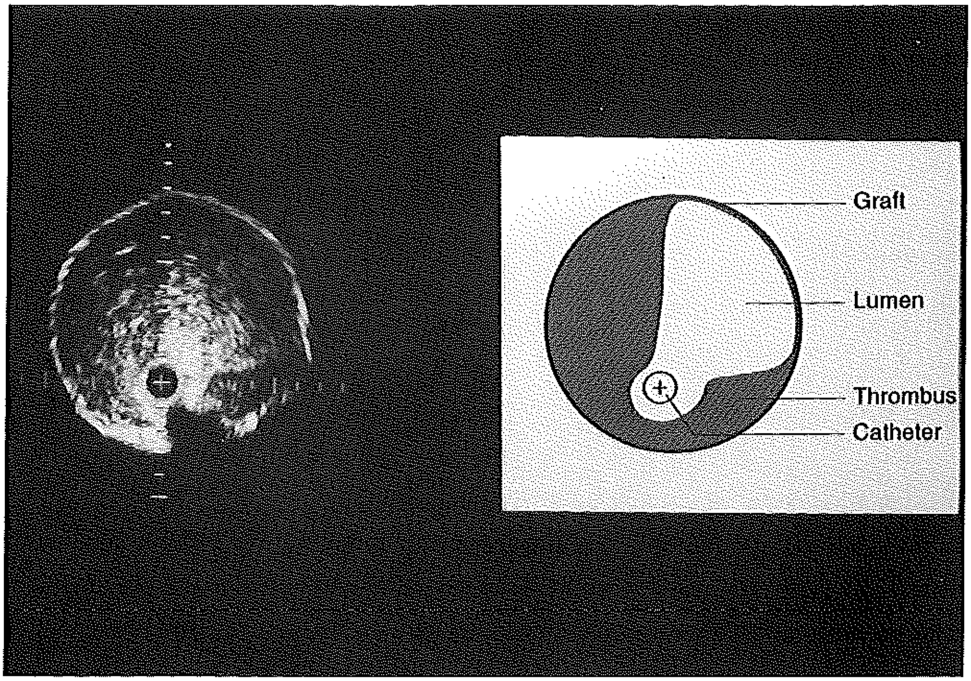

Figure 1. Left: Intravascular ultrasound cross-section showing thrombus formation in a stent-graft. Right: explainary diagram. + = catheter, calibration = 1 mm.

The superficial femoral artery aneurysm in Patient 6 was treated with an 8-cm- long stent-graft composed of 2 Palmaz stents (P308) and ePTFE. After endograft implantation, the aneurysm was still visible on the angiogram, but its cause could not be deduced. IVUS investigation showed the stent-graft to be too short. Moreover, IVUS illustrated a stenosis at the side of a ridge in the ePTFE, which was caused by foreshortening of the stent-graft during dilatation (Fig 2). Neither the stenosis nor the cause of the endoleak could be determined angiographically because stagnant contrast in the aneurysm hampered the view. It was decided to treat the stenosis with an additional stent and to cover the leak with an extra stent-graft. After these additional interventions both the completion angiogram and IVUS revealed a satisfactory result.

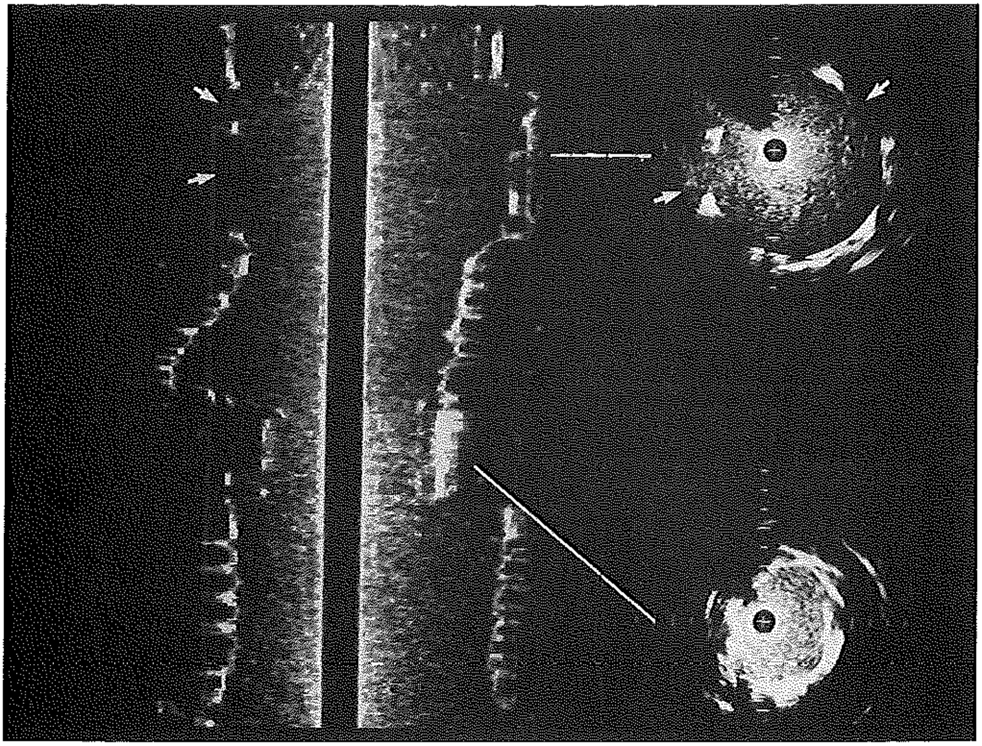

Figure 2. Three-dimensional reconstruction if intravascular ultrasound cross-sections obtained after initial intervention for an aneurysm of the femoropopliteal artery. Right: Upper cross-section shows the too short stent-graft. The arrows indicate the flow through the struts of the uncovered proximal stent into the aneurysm. Lower cross-section shows a ridge within the stent-graft resulting in a stenosis.

Patient 9 suffered from postprandial pain; spiral CT of the abdomen showed an aneurysm of the celiac axis. Through a brachial access, a stent-graft composed of ePTFE and a Palmaz stent was inserted. The control angiogram showed that the aneurysm was not completely excluded and the IVUS study found the stent-graft to be too short. An additional stent-graft was used to exclude the aneurysm (Fig. 3).

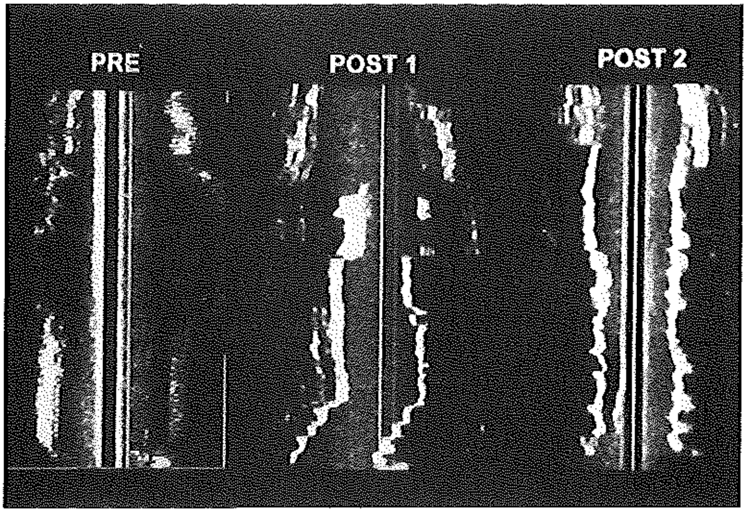

Figure 3. Three-dimensional reconstruction of intravascular ultrasound cross-sections, obtained from a patient with an aneurysm of the coeliac axis. Left panel: pre-intervention images showing the aneurysm. Middle panel: a too short stent-graft, allowing flow into the aneurysm. Right panel: total exclusion of the aneurysm.

DISCUSSION

Relatively few institutions are currently using IVUS for intraprocedural assessment of vascular anatomy and endovascular interventions.[13,14] Although angiography, CT scanning, and magnetic resonance angiography (MRA) play important roles in the pre-operative assessment of vascular disease, individually, these modalities do not always provide accurate information on the diameter of the vessel and the extent of the disease[15].

The present study reports our experience in a group of 17 patients using IVUS imaging before and after endovascular treatment of peripheral aneurysms. The total time to capture the images was not long, and no adverse effects of the IVUS investigation were encountered. Prior to intervention, IVUS evidenced unsuspected stenoses despite pre-operative diagnostic angiography and pressure gradient measurement. These obstructive lesions were serious enough to warrant balloon angioplasty in 2 patients before the planned procedure could be performed.

In 8 of the 17 patients, the stent-graft procedure was deemed successful both on angiography and IVUS imaging. Conversely, in the 9 other patients, both imaging modalities showed inadequate outcomes. However, IVUS alone provided additional qualitative and quantitative data that influenced intraprocedural management in most cases.

While our success with obtaining detailed morphological and quantitative information was high, there were some shortcomings of IVUS. In the area of preprocedural assessment, 3 stent-grafts sized according to IVUS measurements of the aneurysm length were found to be too short. In retrospect, the reasons for this were: (1) correct measurement of length of the aneurysm, but shortening of the stent-graft due to an overly long balloon in one patient; and (2) inaccurate length measurement in a tortuous iliac artery and the celiac aneurysms. Although the IVUS examinations were combined with fluoroscopy and the radiopaque ruler, these measurements remain imprecise. The use of a displacement sensing device, which measures longitudinal displacement of the catheter tip, might prove advantageous in these cases.[16]

It is likely that the angiographically-undetected endograft stenoses appearing on the IVUS imaging could have been demonstrated if fluoroscopy were performed in two directions. However, such a stenosis -due to a ridge within the stent-graft- remains difficult to assess angiographically. The IVUS data gave us insight into the mechanism responsible for this particular stenosis.

Endoleaks detected after deployment of the stent-graft may be seen both angiographically and with IVUS. However, angiographic appreciation of the cause of the leak is problematic. In our study, the intraprocedural IVUS findings were superior to angiography in determining the location and cause of an endoleak, whether it was owing to a too short stent-graft, inadequate apposition that promoted perigraft flow, or rupture of the graft material.

Thrombus seen in a stent-graft can be missed by angiography due to overlying contrast material. In the postoperative period, the presence of thrombus may lead to acute occlusion or distal emboli. Therefore the detection of thrombus may be of paramount importance and we found IVUS once again helpful in identifying the need for thrombectomy in two instances.

Admittedly, the advantage of angiography is its longitudinal display of the vascular anatomy, which is more intuitively appealing to surgeons and radiologists. However, we now have the ability to reconstruct IVUS cross-sections into a 3D format (Figs. 2 and 3). Although these reconstructions may give a better understanding of vessel wall architecture, 3-D reconstruction did not afford additional information to this study.

It is noteworthy that federal regulations regarding maximum radiation exposure must be followed during investigational endovascular procedures[17]. The use of IVUS can significantly reduce fluoroscopy time during these procedures, thus minimizing the duration of radiation exposure to both patients and personnel.

CONCLUSION

Endovascular stent-grafting is an evolving investigative technique that can be executed with better understanding using IVUS imaging. In this series IVUS was safe, accurate and easy to perform in all patients. Although angiography can indicate an inadequate procedure, the additional information provided by IVUS may optimize the procedure, thus increasing the likelihood of an uncomplicated recovery and long-term success.

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CHAPTER 9

SUMMARY / SAMENVATTING

SUMMARY

The development of less invasive, endovascular interventions in the last decade has prompted the need for improved vascular imaging and better diagnostics. Colour duplex, computed tomographic angiography and magnetic resonance angiography can be important for the pre- and postintervention assessment of vascular disease, but these modalities can not be used during intervention. Angiography is the standard imaging technique, also for endovascular procedures, but angiography and fluoroscopy display only a longitudinal silhouette of the vessel lumen, which is insufficient in many cases. Intravascular ultrasound (IVUS) provides histology-like cross-sections of the blood vessel, allowing qualitative evaluation of the plaque and quantitative assessment of lumen, vessel area and plaque area. Moreover, this technique can be used during an endovascular intervention.

In the work presented here, the role of IVUS was evaluated in 2 groups of patients undergoing peripheral endovascular interventions: 1) patients with obstructive vascular disease treated with a stent or endograft, and 2) patients with an aneurysm treated with a stent-graft combination. The contribution of IVUS to improve immediate results, reduce complications, prevent restenosis and increase long-term patency in these patients is evaluated.

Chapter 1 gives an introduction to the scope of the dissertation.

Chapter 2 presents an overview of our experience with over 400 patients in whom IVUS was used to guide a variety of vascular interventions. The various topics addressed include; the advantages of IVUS over angiography, the mechanism of balloon angioplasty and stent placement, aspects of the mechanism of restenosis, and the IVUS predictors of restenosis. It can be appreciated that IVUS is of eminent importance in many endovascular interventions and provides insight in the mechanism of the vascular response following these interventions.

Chapter 3 describes a prospective study of 27 patients treated with a stent for obstructive disease, or a stent-graft combination for aneurysmal disease. Following angiographically optimal stent deployment, IVUS was used to compare the smallest intra-stent lumen area with the dimensions at both stent edges and with the lumen area of the proximal and distal arterial reference sites. This study revealed that in only 14 of the 27 stents the intra-stent dimension was the same as the dimension at the stent edges. Of the remaining 13 stents the intra-stent dimension was smaller than the proximal and/or distal stent edge. In all patients treated with a stent or a stent-graft combination, the resulting smallest intra-stent lumen area was smaller

than the balloon size used (mean difference 32% and 42%, respectively) and smaller than the mean lumen area of the reference sites (mean difference 25% and 23%, respectively). This IVUS study revealed a discrepancy between intra-stent lumen area, area of the stent edges, area of the reference sites and balloon size used; none of these features was detected by angiography. Selection of larger balloon size and/or higher balloon pressures than currently used might be warranted in future clinical applications.

Chapter 4 presents a case report that describes the role of IVUS in assessing the status of stents immediately after implantation in the femoropopliteal artery, and documenting the changes seen at follow-up. The patient received 7 (Palmaz) stents because of an extensive dissection after balloon angioplasty. At 5-months follow-up the patient had recurrent symptoms of disabling claudication caused by restenosis: angiographic and IVUS examination revealed 4 distinct stenoses at the stent junctions. To reveal the changes that occurred, segment-to-segment comparisons were made of the IVUS images obtained immediately after stent placement and at follow-up. The extent of changes seen at the stent junctions was greater than the changes seen within the stents: lumen area reduction, 67% versus 23%; stent area reduction, 26% versus 11%; and intimal hyperplasia, 10.8 versus 3.8 mm^2, respectively. Changes in the non-stented vessel segments were minimal. The conclusions from this IVUS study are that, in addition to intimal hyperplasia, stent area reduction of balloon expandable stents (stent-remodeling) contributes to restenosis in the femoropopliteal artery.

Chapter 5 describes the role of IVUS to document lumen, vessel and plaque area seen after placement of a polytetrafluorethylene (ePTFE) balloon expandable endograft in 12 patients with long segment obstructive femoropopliteal artery disease, and the changes at follow-up (mean 6 months). Corresponding IVUS cross-sections were analyzed for changes seen in the endograft, in the anastomotic segment and in the remote arterial segment. Lumen area change within the endograft (3%) and in the remote arterial segments (6%) was minimal. A distinct increase in lumen area (85%) in the anastomotic segments was determined by the increase in vessel area (42%) and plaque area (15%). This finding is remarkable for an arterial segment that is not manipulated by PTA. From this study, it can be appreciated that vascular remodeling can compensate for intimal hyperplasia at the anastomotic segment of an ePTFE endograft.

Chapter 6 presents the results of endovascular treatment with custom-made stent-grafts in 11 patients with an isolated or para-anastomotic iliac aneurysm. The interventions were guided by both angiography and IVUS. The main advantage of this endovascular treatment is that the aneurysm can be treated from a remote site, eliminating the need for and potential danger of extensive dissection. Other advantages are minimal local trauma, decreased blood loss, rapid postoperative recovery and shorter postoperative hospitalisation.

Chapter 7 describes the results of the preliminary use of stent-grafts for the treatment of femoropopliteal artery aneurysms. In all 10 patients the procedures were guided by both angiography and IVUS. In 2 patients a conversion to an open surgical procedure was mandatory. In 8 patients the procedure was completed successfully. In 3 of these 8 patients an additional intervention during the initial procedure was required. In the early postoperative period 2 failures were encountered. During follow-up of the remaining 6 patients one stent-graft occluded and in one patient a stenosis of the distal attachment system was found. From this study it can be concluded that endovascular stent-grafting of aneurysms of the femoropopliteal artery is a feasible but still experimental technique that should be restricted to a carefully selected group of patients. IVUS investigation provides additional information to optimize the procedure, based on better understanding of the extent of the disease and of the problems encountered following intervention.

Finally, in **Chapter 8** the potential diagnostic information of intraoperative IVUS, in 17 patients undergoing endovascular stent-grafting for peripheral aneurysm, is evaluated. In all patients, IVUS was used to measure the diameter of the proximal and distal neck and the length of the aneurysm: balloon and stent-graft sizes were selected based on these measurements. In 9 of the 17 patients, both angiography and IVUS showed inadequate results, necessitating 12 additional procedures. In these patients intraprocedural IVUS was superior to angiography in providing vital information to aid in the selection of additional interventions. IVUS monitoring was a useful adjunct to angiography when the initial procedure was unsatisfactory and/or when angiographic studies were inconclusive.

SAMENVATTING

De ontwikkeling van minimaal invasieve, endovasculaire interventies van de laatste 10 jaar creëerde een behoefte aan betere vasculaire diagnostiek. Kleuren duplex, computer tomografische angiografie en magnetische resonantie angiografie kunnen een belangrijke diagnostische rol vervullen bij vaatafwijkingen, maar deze vormen van diagnostiek kunnen niet worden toegepast tijdens een interventie. Angiografie is de standaard techniek voor het afbeelden van vaatafwijkingen, ook tijdens endovasculaire interventies. Echter zowel angiografie als doorlichtingstechnieken tonen slechts een longitudinaal silhouet van het lumen van het bloedvat. Dit is vaak niet voldoende. Intravasculaire echografie (IVUS) levert een op histologie-lijkende dwarsdoorsnede van het bloedvat op, waardoor *kwalitatieve* evaluatie van de atheromateuze plaque en *kwantitatieve* metingen van het lumen, bloedvat en plaque oppervlak mogelijk zijn. Deze techniek kan ook tijdens endovasculaire interventies worden toegepast.

In dit proefschrift wordt de rol van IVUS beoordeeld in 2 groepen patiënten, die een perifere endovasculaire interventie ondergaan: 1) patiënten met obstructief vaatlijden behandeld met een stent of endograft, en 2) patiënten met een aneurysma behandeld met een stentgraft combinatie. De bijdrage van IVUS aan het verbeteren van primaire resultaten, verminderen van complicaties, voorkomen van restenose en verbeteren van de lange termijn resultaten bij deze patiënten wordt bestudeerd.

Hoofdstuk 1 geeft een introductie van de inhoud van dit proefschrift.

Hoofdstuk 2 geeft een overzicht van de ervaring van ons instituut bij meer dan 400 patiënten, waarbij IVUS werd gebruikt bij een scala van endovasculaire interventies. Verschillende onderwerpen worden behandeld: de voordelen van IVUS boven angiografie; het mechanisme van ballon angioplastiek en stentplaatsing; aspecten van het mechanisme van restenose; de voorspellende waarde van IVUS aangaande restenose. Geconcludeerd mag worden dat IVUS een belangrijke rol kan spelen bij een variëteit van endovasculaire interventies en tevens inzicht geeft in het reactiepatroon van het bloedvat op deze interventies.

Hoofdstuk 3 beschrijft een prospectieve studie van 27 patiënten die werden behandeld met een stent voor stenoserend vaatlijden of een stent-graft combinatie voor aneurysmatisch vaatlijden. Na een angiografisch optimale ontplooiing van de stent werd IVUS gebruikt om het kleinste lumen oppervlak in de stent te vergelijken met de dimensies van de stent aan beide uiteinden en het lumen oppervlak in het proximale en distale referentiesegment. Deze studie toonde aan dat slechts in 14 van de 27 gevallen het lumen oppervlak in de stent gelijk was aan het oppervlak in de stentranden. In de overige 13 stents was het lumen oppervlak in de stent kleiner dan het oppervlak in de proximale en/of distale stentrand. Bij zowel alle patiënten behandeld met een stent als bij de patiënten behandeld met een stent-graft combinatie was het kleinste lumen oppervlak in de stent kleiner dan het oppervlak van de gebruikte ballon (mediaan verschil respectievelijk 32% en 42%) en kleiner dan de oppervlakte van de referentiesegmenten (mediaan verschil respectievelijk 25% en 23%). Deze IVUS studie heeft aangetoond dat er een discrepantie bestaat tussen het oppervlak in de stent, het oppervlak in de stentranden en het oppervlak van de gebruikte ballon, hetgeen niet kon worden aangetoond met angiografie. Selectie van een grotere ballon en of hogere druk lijkt derhalve aangewezen bij toekomstige toepassing.

Hoofdstuk 4 beschrijft in een patiëntencasus de rol van IVUS bij het beoordelen van stents direct na ontplooiing in het femoropopliteale traject en bij het documenteren van de veranderingen die bij follow-up werden gevonden. Bij deze patiënt werden 7 (Palmaz) stents geïmplanteerd in verband met een uitgebreide dissectie na ballon angioplastiek van de arteria femoralis superficialis. De patiënt kreeg recidief klachten als gevolg van restenosering na 5 maanden follow-up. Angiografie en IVUS toonden een viertal stenoses aan op de stentovergangen. Om de opgetreden veranderingen in de stent aan te tonen, werden de IVUS beelden verkregen direct na de stentplaatsing en de beelden bij follow-up met elkaar vergeleken van per overeenkomend segment. De uitgebreidheid van de veranderingen ter plaatse van de overlap van twee stents bleek groter te zijn dan van de veranderingen in het midden gedeelte van elke stent: lumen oppervlak verkleining, 67% versus 23%; stent oppervlak verkleining, 26% versus 11%; en intima hyperplasie 10,8 mm^2 versus 3,8 mm^2. De veranderingen in het niet behandelde vaatgedeelte waren minimaal. Op grond van deze IVUS studie kan worden geconcludeerd dat naast intima hyperplasie, remodelleren van (ballon expandeerbare) stents kan bijdragen aan restenosering in het femoropopliteale traject.

Hoofdstuk 5 beschrijft een IVUS studie waarin bij 12 patiënten met obstructief vaatlijden in een lang (>5 cm) vaatsegment het lumen, bloedvat en plaque oppervlak werd gemeten direct na behandeling met een polytetrafluorethyleen (ePTFE) ballon-expandeerbare endograft en tevens bij follow-up (gemiddeld 6 maanden). Corresponderende IVUS dwarsdoorsneden werden beoordeeld op veranderingen in lumen, bloedvat en plaque oppervlak gemeten in de endograft, in het anastomotische vaatsegment en in het vaatsegment verder verwijderd van de endograft. De verandering in het lumen van de endograft (3%) en lumen van het verder verwijderde vaatsegment (6%) was minimaal. De duidelijke toename in het lumen oppervlak (85%) gezien in het anastomotische vaatsegment werd bepaald door de toename van zowel het oppervlak van het bloedvat (42%) als het oppervlak van de plaque (15%). Dit is een opmerkelijke bevinding bij vaatsegmenten die niet zijn gemanipuleerd door ballon dilatatie. Deze studie toont aan dat intima hyperplasie in anastomotische vaatsegmenten van een ePTFE endograft gecompenseerd kan worden door remodelleren van het bloedvat

Hoofdstuk 6 beschrijft de resultaten van endovasculaire behandeling met zelfgemaakte stentgrafts (bestaande uit Palmaz stents en een ePTFE graft) bij 11 patiënten met een geïsoleerd of para-anastomotisch aneurysma van het *iliacale* traject. De procedures werden gestuurd op basis van de gegevens van zowel angiografie als IVUS. Het grote voordeel van de endovasculaire behandeling is dat het aneurysma via een kleine incisie op afstand behandeld kan worden zonder een uitgebreide dissectie en de daarmee gepaard gaande risico's. Andere voordelen van deze behandeling zijn het minimale lokale trauma, het verminderde bloedverlies, de kortere postoperatieve hersteltijd en de kortere opnameduur.

Hoofdstuk 7 beschrijft de resultaten van het experimentele gebruik van stent-grafts bij de behandeling van 10 patiënten met een aneurysma in het *femoropopliteale* traject. De procedures werden gestuurd verricht op geleide van de gegevens van angiografie en IVUS. Bij 2 patiënten was een conversie naar een open chirurgische procedure noodzakelijk. Bij 8 patiënten kon de procedure succesvol worden voltooid. Bij 3 van deze 8 patiënten was het noodzakelijk om direct aansluitend op de initiële procedure een additionele interventie uit te voeren. In de vroege postoperatieve periode werden 2 mislukkingen gezien. Gedurende de follow-up van de overige 6 patiënten occludeerde de stentgraft bij één patiënt en werd bij een andere patiënt een stenose waargenomen ter plaatse van de distale bevestigingsstent. De conclusie van deze studie was dat endovasculaire behandeling van aneurysmata in het femoropopliteale traject mogelijk is, maar dat deze experimentele behandeling voorbehouden dient te worden aan een zorgvuldig geselecteerde groep patiënten. De IVUS gegevens verschaften additionele informatie waarmee de procedure geoptimaliseerd kon worden door een beter inzicht in de uitgebreidheid van de afwijking en de ontstane problemen tijdens de interventie.

Tenslotte wordt in **hoofdstuk 8** de potentiële diagnostische waarde van IVUS samengevat en beoordeeld bij 17 patiënten met een perifeer aneurysma, behandeld met een endovasculaire stent-graft. Bij alle patiënten werd IVUS gebruikt om de diameter van de proximale en distale hals en de lengte van het aneurysma vast te stellen. De diameters van de ballon en van de stent-graft werden gekozen aan de hand van deze gegevens. Bij 9 van de 17 patiënten toonden de angiografie en IVUS beiden een niet bevredigend resultaat, hetgeen leidde tot 12 additionele behandelingen. IVUS, gebruikt tijdens de interventie, was beter dan angiografie ten aanzien van het verschaffen van essentiële informatie voor de keuze van additionele behandeling. De gegevens van IVUS waren een nuttige aanvulling wanneer de initiële interventie een niet bevredigend resultaat liet zien en/of wanneer de angiografie niet conclusief was.

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